*In memory of*

JOHN H. MUSSER, JR.

(1883-1947)

*Distinguished Physician and Leader*
*in American Medicine*

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# INTERNAL MEDICINE

*Its Theory and Practice*

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WITH 80 CONTRIBUTORS

*236 Illustrations and 10 Colored Plates*



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# Preface

The aim of this book is to present in one volume a comprehensive survey of the entire field of internal medicine. To this end many distinguished teachers and authorities in medicine have contributed to this edition of the Musser text in order to enlarge the work and bring it up to date.

Since the publication of the 4th edition in 1944 our knowledge of medicine has so greatly increased that it has been necessary to rewrite many chapters and add new ones.

The book is designed primarily for the medical student and the physician engaged in general practice. Every effort has therefore been made to present the clinical aspects of disease clearly and in detail. And since understanding the clinical manifestations of disease requires understanding physiology, biochemistry and pathology, the contributors have endeavored to integrate these sciences with bedside medicine.

The book is arranged in seven sections. The first section deals with infectious diseases, the second with diseases due to physical and chemical agents, the third with diseases of nutrition, metabolism and the endocrine glands, the fourth with diseases of allergy and collagen diseases, the fifth with systemic diseases, the sixth with geriatrics and rehabilitation, and the seventh with diseases of the nervous system.

The chapters on genetics, geriatrics, rehabilitation and psychosomatic medicine and the section on the general adaptation syndrome are special features of this edition. These, it is thought, contribute to the understanding of the modern conception of the "whole" patient.

Special emphasis has been put on modern therapeutic procedures which, in the various authors' experience, are of proved value.

The editor wishes to avail himself of this opportunity to express his appreciation to his son, Dr. George T. Wohl, who in the capacity of associate editor has rendered invaluable aid in the preparation of the book.

He also would like to thank Doctors Herman Beerman, Heinrich Brieger, William Ehrich, George M. Eisenberg, Harold I. Israel, Harold Jeghers, Richard A. Kern, Morton Klein, A. C. LaBoccetta, John Lansbury, Milton Lewis, Matthew T. Moore, Hugo Roesler, M. Michael Sigel, Martin J. Sokoloff and Earle H. Spaulding for their generous help. Credit is due to Dr. Leopold Z. Goldstein for the preparation of the index.

The editor wishes further to express his thanks to the many authors, each of whom gave of himself willingly; to the publishers for their constant encouragement and cooperation; and to Mr. LeRoy Smith, Jr., who has helped us immeasurably with the editorial work. Lastly, the editor desires to express his gratitude to Mrs. Clara Wein, who has been faithful in the arduous secretarial work entailed in the preparation of this volume.

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# APPROACH TO THERAPY

## INTRODUCTION

We are witnessing great advances in therapy today Sulfanilamide and its derivatives are conquering infections of various types, newer forms of insulin have been perfected to bring greater comfort to the diabetic, in the treatment of the psychoses gratifying results have followed the use of newer remedies Pyrexial therapy the sex hormones, the vitamins a variety of safer anesthetics reflect many advances in other fields The treatment of diseases of the heart has not lagged behind Today more can be done for the cardiac invalid than was possible a decade ago A better understanding of the mechanism of heart failure, a clearer concept of the use of digitalis and the introduction of newer diuretics are only a few of the factors that enable the modern physician to bring a degree of relief to cardiac patients not dreamed of at the beginning of the present century

The appearance on the scene of many laboratory methods of precision characterizes the modern era While these attract a considerable amount of the attention of research investigators they should not be allowed to replace the older methods of physical examination We must realize that even the foremost among these electrocardiography and roentgenography taken together cannot furnish the amount of information that may be obtained from a carefully taken history and a thorough physical examination All laboratory methods have great pitfalls for the ones who in the hurry that is typical of modern times lean upon them too heavily Laboratory methods of precision are only aids to be sought in establishing a diagnosis that is suggested after all the facts in the case have been collected recorded and fully evaluated If this procedure is always followed often the diagnosis will stand out so clearly that there will be scant need for a number of expensive laboratory tests For example, a good clinician will not permit a patient who has a precordial friction rub following an attack of agonizing chest pain to be moved any distance for the sole purpose of obtaining an electrocardiogram Nor will a roentgen examination add a great deal to the patient s diagnosis when the Wassermann reaction is positive the pulse is of the Corrigan type and the apex beat is visible in the midaxillary line

In some instances however after all available data are carefully considered laboratory procedures will be necessary to help clarify a diagnosis The Wassermann for example is a great help in making a decision as to therapy in a patient of 40 whose only lesion appears to be aortic regurgitation and whose past history is negative for rheumatism and syphilis In

some cases of suspected coronary occlusion the entire examination of the patient may be negative and the diagnosis will be revealed only in the chest leads of the electrocardiogram Often the electrocardiogram may be the sole evidence of the presence of acute myocarditis However the instances are few where the laboratory acts as the cornerstone in diagnosis An attempt should be made in every case to arrive at the cardiac diagnosis unaided for in this way the ability of the physician to diagnose heart disease will increase with his experience and in emergencies he will find that he can direct treatment efficiently when laboratory aid is unavailable

## THE HISTORY

The best approach to therapy is a brief consideration of the methods commonly employed in arriving at a diagnosis of heart disease Careful history taking remains the most important but often the most neglected feature of the entire examination It should never be relegated to an assistant for impressions that may be essential to diagnosis are made in taking the history Furthermore in certain types of heart disease the diagnosis can be made on the history alone I make a rule to take a long history but to write a short one

**The Patient s Description** It is wise to permit the patient to tell his own story and allow him plenty of time to review it completely I share the patient s dislike for any system that entails the routine asking of a large number of questions by an office assistant who fills in a printed form, but perhaps this is only a personal expression of rebellion against the present day system of regimentation In any event stereotyped questions usually receive the same type of answers and although they may be very useful in subsequent research this system deprives the physician of the opportunity of witnessing in an informal friendly interview the unfolding of the patient s personality with the story of his symptoms Frequent interruptions confuse and irritate the patient and usually inhibit the growth of confidence in the physician that is so essential at the first interview Let the patient talk It is an easy matter to jot down roughly the important features of the narrative and either dictate or rewrite the history later Of course this freedom in the telling should not be allowed some patients who deal at length with multiple and irrelevant issues However even in these cases much can be learned concerning the probable presence or absence of heart disease if the physician trains himself to be a good listener Further amplification of important symptoms lightly touched upon by the patient may be obtained by asking a few direct questions at the end of the interview As many as possible of the adjectives used by the patient in describing an important symptom should be recorded using quotation marks The description of the complaint at a subsequent visit by the use of the patient s own phrases establishes confidence in the physician This is particularly true in regard to the variety of expressions used by patients in describing chest sensations Many are fearful of the diagnosis of angina yet desire

to give the physician the most accurate account possible of the chest symptom consequently their descriptions may be rich in clarifying similes

**The age of the patient** is a most important fact in itself in cardiovascular diagnosis Certain types of heart disease are more frequent in certain age groups For example, under two years of age it is unusual to meet any form of heart disease other than congenital After this age and during the first decade of life we have to consider rheumatic carditis plus congenital heart disease From this time until 40 rheumatic heart disease dominates After 40, cardiovascular syphilis becomes a consideration and between 40 and 60 coronary and hypertensive cardiovascular disease predominate while congenital defects are very rare and the rheumatic lesions very infrequent From 60 to 80 coronary or arteriosclerotic and hypertensive varieties hold the stage these types are usually present as the final curtain falls

**The sex** of the patient is an important consideration in etiology For example it is a statistical fact that the coronary and syphilitic types of heart disease occur with greater frequency among males Calcific aortic stenosis likewise affects men more often than women Rheumatic and hypertensive heart disease however seem to claim an equal number of victims from both sexes Thyrotoxic heart disease on the other hand is more prevalent among women

**Hereditary Factors** It is very important to inquire carefully into the causes of death of all near relatives From the frequency with which I have encountered rheumatic hypertensive and coronary artery disease in members of the same family it appears that the incidence of these diseases is influenced by hereditary factors A positive family history always adds weight to the diagnosis of angina when the cause of an atypical chest pain in an active business man in middle life is considered

**The past medical history** has a direct bearing on the type of heart disease that may be present If several typical attacks of rheumatic arthritis occurred in childhood evidence enough is at hand to suspect this type of cardiac involvement Chorea may be viewed in the same light Growing pains quinsy tonsillitis may or may not be rheumatic in nature but provide evidence that should be weighed carefully 'Usual diseases of childhood is a routine meaningless phrase that appears on nearly all hospital records Diseases if recalled should always be listed by name Diphtheria and scarlet fever usually have no effect in later years on the cardiac status of the patient

**Syphilis** Inquiry as to the presence or absence of a syphilitic lesion should always be made toward the end of the interview This question is a very important one particularly in patients in middle life who exhibit signs of aortic disease It should never be asked in a tone that invites denial If the patient is a woman a visible primary lesion may not have been present In this event clues will have to be sought carefully during the subsequent physical examination

### Cardiac Symptoms

In each patient it is important to attempt to establish accurately the date of the first appearance of cardiac symptoms A brief summary of the progress of each symptom to the date of the examination should follow Cardiac symptoms of importance are chest pain abnormalities of breathing or dyspnea and palpitation They are described differently by each patient because the nervous mechanism that detects and interprets them is a factor that shows considerable individual variation In no case will the symptoms be directly proportional to the amount of structural change producing them Moreover they may all be present in an oversensitive individual in the absence of any type of organic cardiac disease They *may appear at one time and not at another for example, when fatigue* enters the picture and lowers the patient s threshold of perception

Chest pain is the most important of all cardiac symptoms Care should be exercised in its description in the history for in a few instances it may be the only positive finding in the entire case record If the chest pain or oppression is transient and definitely related to exertion, and relieved by rest and nitroglycerine, the diagnosis of coronary disease is at once suggested Pain having the same qualities and significance may be experienced in regions distant from the heart—for example in the neck jaw shoulder, arms or even the abdomen

The pain that accompanies occlusion of a coronary artery or any of its branches usually can be differentiated clinically from the pain of angina When occlusion occurs, the transient pain of angina gives way to a prolonged agonizing type of pain that is accompanied generally by marked changes in the appearance of the patient The pallor sweating and shock that accompany occlusion are important points to elicit and record if as is usually the case the person who witnessed the attack accompanies the patient to the office

Chest pain may be a feature of other types of heart disease A dull precordial ache is complained of by patients suffering from effort syndrome It often accompanies the overactive heart of thyrotoxicosis and may be present in patients who have cardiac hypertrophy from any cause but particularly if it is of the hypertensive type The nervous system of some patients is unfortunately very closely in tune with the cardiac action Consequently irregularities such as frequently recurring premature beats will be readily detected and may produce painful stimuli At times they may be the cause of knife like pains in the cardiac area Acute pericarditis may produce a precordial pain that is increased by respiration owing to the extension of the inflammatory process to the outer layer of the pericardium and thence to the pleura or diaphragm If effusion follows the pain may disappear entirely or it may give way to a dull precordial ache

Aortic aneurysm by its growth and erosion is responsible for a severe and constant type of chest pain The pain produced by dissection of an

aortic aneurysm is perhaps the most excruciating variety experienced by man It is sudden in onset, of maximum intensity from the start and is referred to the front or side of the chest or to the abdomen Patients often describe it as 'tearing' It may however, be confused with the pain of coronary occlusion in some cases (page 523)

**Dyspnea** has many causes, but there are usually three types commonly described in relation to diseases of the heart In early cardiac failure the patient becomes conscious of the respiratory act As the lungs become engorged following left ventricular failure, reflexes to the respiratory center usually increase the rate of breathing As failure progresses dyspnea may be present at complete bed rest We use the term 'orthopnea when the dyspnea is extreme and the respiratory act demands the patient s whole attention and much of his failing strength The patient with orthopnea is forced to sit up in bed in order to employ the accessory muscles of respiration as well as the effects of gravity to relieve the over loaded pulmonary circulation

An increasing degree of dyspnea u ually parallels the loss of cardiac reserve and is valuable in estimating prognosis in any patient under treat ment The amount of breathlessness that follows the same task assigned at each visit should always be carefully observed and recorded

**Cardiac Asthma** The sudden attack of dyspnea that often follows acute failure of the left side of the heart during sleep when the head and chest are low is known as paroxysmal cardiac dyspnea or cardiac asthma These distressing episodes frequently occur toward the end of life when the types of heart disease that place the extra load on the left ventricle are common It is important to record the date of onset of these seizures in the history

**Cheyne Stokes Respiration** In the advanced stages of some types of heart disease poor cerebral circulation following sclerosis and declining cardiac reserve markedly affects the respiratory center Periods of apnea or cessation of breathing alternate with periods of increased breathing or hyperpnea producing the well known clinical picture of Cheyne Stokes respiration Relatives who are constantly in attendance often give accurate descriptions of this symptom which when marked, indicates a poor prognosis

**Palpitation** or consciousness of the beating of the heart is a very common but a much less important complaint The patient usually classes several types of cardiac happenings under this heading which must be carefully sorted out when the history is taken The occasional disturbances of the heart s rhythm caused by extrasystoles reach consciousness and are classed as palpitation The sudden onset of paroxysms of fibrillation flutter or tachycardia are usually felt by the patient and also described under the heading of 'palpitation Consequently when palpitation is the symptom question the patient in detail to bring out the exact nature of the disorder Palpitation is a very common symptom in effort syndrome and thyrotoxicosis Many of the patients complaining of palpitation will be found

to have no underlying cardiac disease Consciousness of the heart's action is a very common complaint among those suffering from anxiety neurosis

**Syncope vertigo and faintness** may all be directly associated with some form of heart disease Different degrees of cerebral anemia due to slowing of the pulse or a fall in blood pressure or both may be responsible In patients with aortic regurgitation and stenosis and varying degrees of heart block vertigo and syncope are important symptoms to elicit Occasionally sudden occlusion of a coronary artery may cause syncope Very rapid cardiac rates when coronary filling is incomplete may be followed by a loss of consciousness On the other hand syncope may occur after any mild exertion excitement or emotion in a susceptible person The mechanism here is either vagal or vasomotor or a combination of these two elements

Finally many gastro intestinal symptoms (anorexia gas nausea upper abdominal pain) may be complained of by the cardiac patient They may arise in the course of coronary disease or may accompany congestive failure Hoarseness is caused in rare cases by the presence of a large left atrium secondary to mitral stenosis or may follow pressure of an aortic aneurysm on the recurrent laryngeal nerve Cough and hemoptysis are not uncommon symptoms associated with the pulmonary congestion that accompanies failure of either ventricle Pulmonary symptoms often predominate in the later stages of mitral disease

## THE EXAMINATION OF THE PATIENT

The physical examination of every patient begins as soon as he enters the physician's office The speech the manner and the emotions as the history is given reflect at once the patient's mental background These impressions should always be noted for they are very helpful in the evaluation of the cardiac symptoms In making complete physical examinations it is wise for the beginner to adopt an orderly system and carefully record all findings With experience and constant practice the physical status of a patient may be determined very quickly and only the positive findings need be recorded Confining the physical examination to the chest will lead to grave errors in diagnosis since signs in other regions at a distance from the heart may be most important in the discovery of the kind of heart disease present

**The type of breathing** and the respiratory rate are important observations to make Orthopnea seizures of cardiac asthma breathing of the Cheyne Stokes type all give warning of grave danger ahead whereas the patient who is frequently compelled to pause to take an unusually deep breath (sighing type of respiration) is usually giving a valuable hint that suggests the absence of serious cardiac disease

**The color of the face and lips** as well as the distribution of this color should be noted In patients with mitral disease purplish red patches of color (malar flush) may be observed Marked pallor of the face may be

seen in patients suffering from coronary sclerosis and at times in patients with aortic disease

**Cyanosis** is due to change in the character of the circulating blood appearing when the capillary blood contains more than five per cent of reduced hemoglobin It is seen in 35 to 50 per cent of the cases of congenital heart disease and occurs when over one third of the output of the heart is shunted from the right to the left side without passage through the lungs Advanced mitral lesions interfere with pulmonary circulation and cyanosis may follow improper oxygenation Hydrothorax and edema of the lungs both interfere with proper pulmonary aeration On the other hand the extreme cyanosis found in patients with pulmonary sclerosis

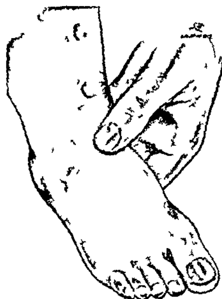


FIG 1 The pitting edema of congestive cardiac failure

(black cardiacs) is often caused by the pulmonary disease entirely and not by any cardiac defect Heart failure from any cause may produce cyanosis since the slow circulatory rate in this condition produces capillary stagnation and greater reduction in the hemoglobin

**Edema** is an important sign in heart disease It may develop suddenly or slowly and may vary from a slight pitting of the ankles appearing only at night to a generalized anasarca As heart failure develops edema is first noted in the lower extremities toward the end of the day while in patients confined to bed it may appear over the sacral region The edema of the feet that accompanies early cardiac failure tends to disappear after a night's rest and to recur at the end of the next day The condition may increase until pitting (Fig 1) is present at all times Fluid may then

accumulate in the pleural cavity (hydrothorax), in the abdomen (ascites) (Fig 2) and finally become generalized (anasarca)

Cardiac edema is a symptom of hypertension in the capillary bed and varies *with the venous pressure* It accompanies right heart failure and conditions that prevent proper diastolic filling (chronic constrictive peri carditis) Left heart failure and shock are not accompanied ordinarily by edema because they produce a diminution of the blood flow that is not associated with increase in capillary pressure

Edema of the feet may be present in renal disease Such edema is usually worse in the morning and is associated with marked swelling of the face In the later months of pregnancy edema of the feet may be present owing

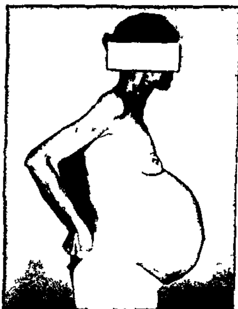


FIG 2 Ascites accompanying congestive cardiac failure

to uterine pressure on the large veins (page 445) Other abdominal tumors may also cause edema and lead the physician to suspect the presence of cardiac disease Severe grades of anemia can produce all the symptoms of cardiac disease, including edema Myxedema (see Fig 142) will rarely be mistaken for the edema of cardiac failure because of the thickening of the *skin that accompanies this deficiency state and the failure of the extremities* to show pitting on pressure Rarely Milroy s disease (persistent hereditary trophedema) may simulate cardiac edema but its presence in several gen erations of the family and the demarcation between swollen and nonswollen parts serve to make the distinction evident In beriberi of the wet type (see Fig 163) a generalized edema may occur In this disease an accumula tion of fluid in the heart muscle has also been described

INSPECTION

**Eyes** In the physical examination of the patient inspection of the eye grounds is commonly omitted This is unfortunate when we consider the amount of information that may be obtained by one familiar with the use of an ophthalmoscope Many times the mark of a previously existing hypertension will be seen in the retina and this will support the diagnosis of hypertensive cardiovascular disease if the blood pressure happens to be low at the time of the examination The recent use of slit lamp inspection of the small capillaries of the conjunctiva has shown that these vessels exhibit changes in their structure suggestive of hypertension even earlier than the arterioles of the retina Gross inspection of the conjunctiva for petechial hemorrhages is also important in cases where subacute bacterial endocarditis is suspected

The presence of exophthalmos and related eye signs of hyperthyroidism may be important observations in explaining the cause of a persistent tachycardia The pupillary reflex to light as well as irregularity of the pupils may lend support to a diagnosis of syphilis It is well to keep in mind the fact that over 50 per cent of the cases of cardiovascular syphilis are complicated by neurosyphilis

**Infection** about the margins of the teeth should be carefully noted as well as all nonvital and abscessed teeth The pharynx should be inspected for infected lymph follicles and the tonsils carefully examined for evidence of hypertrophy or infection The condition of the anterior pillars is important when considering tonsillar infection and the presence of tags may have a decided influence in favoring the recurrence of the upper respiratory infections that are so dangerous in rheumatic subjects The lymph nodes draining all these structures should be palpated carefully

**Neck** Examination of the neck furnishes many important clues Careful inspection of the vessels may permit the observer to diagnose the nature of the cardiac arrhythmias For example detection of abnormal venous pulsations in the jugular veins of a patient with a ventricular rate of 40 may clinch the diagnosis of heart block while a more rapid series of waves may be seen in the jugulars in cases of auricular flutter The engorgement and pulsation of the jugulars in cases of congestive failure and chronic constrictive pericarditis (see Fig 82) signify delay in the return of the venous blood to the heart and increase in the pressure on the venous side Consequently it is evident that a close study of the neck veins is a great aid in the diagnosis and treatment of the cardiac patient

Increased pulsations in the carotid arteries occur in patients suffering from aortic regurgitation hypertension and aneurysm In the latter instance tracheal tug may also be palpable The region of the carotid sinus is important since pressure here in hypersensitive patients may cause syncope (page 578)

**Chest** Careful inspection of the chest of the cardiac patient will richly reward the examiner Slight but definite bulging of the left side of the

precordium (Fig 3) usually indicates cardiac disease in youth before the calcification of the costal cartilages consequently either rheumatic heart disease or a congenital defect should be suspected Kyphosis scoliosis and at times depressed sternum or funnel chest are important clues since they may so compress and displace the heart as to interfere seriously with its

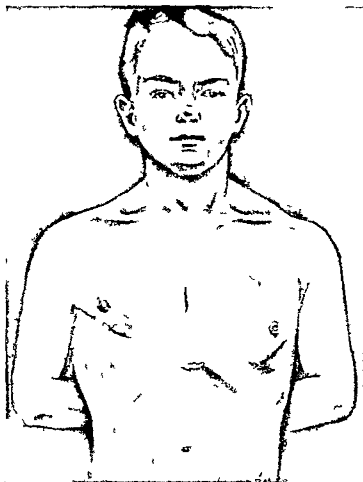


Fig 3 Precordial prominence in a child caused by a greatly enlarged heart

action In thin chested individuals an apex beat visible in the sixth inter space beyond the midclavicular line is evidence of enlargement of the left ventricle Right ventricular enlargement is suggested by pulsations in the third and fourth interspaces to the left of the sternum Retraction of the whole thoracic wall about the region of the cardiac apex is suggestive of an adherent pericardium Although rare sights today pulsating masses on the anterior thoracic wall suggest aneurysm of the aorta (see Fig 91)

## Palpation

**Thrills** palpable over any area of the chest are important indications of narrowing valvular orifices They are best appreciated by light palpation A diastolic thrill over the region of the cardiac apex suggests mitral stenosis When a rough systolic murmur is heard over the second and third interspaces to the right of the sternum, the presence of a systolic thrill in this region will add considerable weight to the diagnosis of aortic stenosis Rarely an aortic aneurysm will produce a systolic thrill in the same area A thrill over the region of the third interspace to the left of the sternum points to a congenital defect of the interventricular septum When a thrill is felt over the pulmonary valve area it is generally associated with stenosis of this valve and is usually congenital in origin When a continuous thrill is present in this area accompanied by loud systolic and diastolic murmurs a patent ductus arteriosus may be suspected

## Percussion

In spite of many opinions to the contrary in literature I still believe that percussion is a worth while method for estimating cardiac size However, the necessary degree of skill in this branch of physical diagnosis can only be acquired by constant daily practice In the majority of patients the size of the heart can be approximately obtained without resorting to more accurate roentgen methods Corvisart[73] [4] said,

> Percussion of the thorax is the best touchstone we have to investigate or at least clarify our knowledge concerning many of the lesions of this cavity By its means we can demonstrate an increase in the volume of the heart one may even go so far as to estimate the severity of the lesion it cannot be used too frequently by means of tactile sense a deaf person may make use of percussion

**The left cardiac border** should be percussed first The change of note in normal patients will be found to occur 8 to 9 cm to the left of the mid sternal line in the fifth interspace When this border is determined the midclavicular line can be indicated on the chest surface and the relationship noted The remainder of the left border of the heart can then be completed percussing in each interspace from axilla to sternum until a change in note from resonance to dulness is heard Care should be taken in the third interspace for lesions affecting the pulmonary artery and pulmonary conus (mitral stenosis patent ductus arteriosus) may cause an increase in the diameter at this level A change may be noted by careful percussion even in cases where the apex beat is in a normal position

**Right Border** In the percussion of the right border of cardiac dulness more difficulty is usually encountered This border follows the right sternal margin to the fourth or fifth interspace where it bulges slightly outward and with care can be percussed for a maximum distance of 5 cm from the midsternal line Percussion over the sternum usually sends the whole

structure into vibration and in the presence of this resonance localization of the heart border is impossible Likewise fine differences in the percussion note here are scarcely appreciated in patients with emphysema and obesity In determining cardiac size in these cases the roentgen methods have their greatest usefulness

If in the course of the examination, I fail to locate the apex beat I always attempt to outline the heart by percussion before proceeding with fluoroscopy The opportunity of checking the result by an orthodiagram keeps alive my belief in the value of ordinary percussion This special training

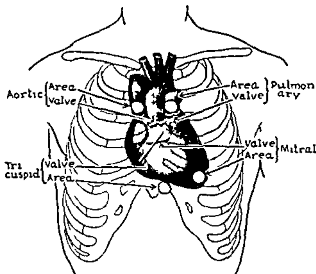



FIG 4 The valve areas and the anatomic location of the heart valves

of the senses of touch and hearing proves a valuable asset at the bedside far from the roentgen laboratory The determination of heart size is the most important single feature of the examination of the cardiac patient, since an enlarged heart is usually a diseased heart

**Aorta** While I believe that the heart dulls somewhat the ringing resonance sufficient to permit its outline by percussion I do not hold the same opinion in regard to the great vessels at the base when they are normal in size If the aorta is inspected in the cadaver it will be seen to arch in a direction away from the chest wall In addition the vessels at the base of the heart are surrounded by lung tissue Consequently unless the aorta is greatly enlarged I doubt my ability to indicate its diameters with any degree of accuracy by percussing the anterior chest wall

## Auscultation

In auscultation of the heart it is important to examine the patient both in the upright and recumbent positions Often certain types of murmurs will be heard only after exercise when the patient is lying on the left side

Auscultation should be carried out over all the cardiac valve areas (Fig 4) I prefer to use the combination type of stethoscope (Fig 5) since murmurs not audible with the bell type of chest piece may at times be clearly heard when the Bowles attachment is used The faint murmur in early mitral stenosis usually is heard best when the bell of the stethoscope is used, while the soft diastolic murmur of aortic insufficiency is detected best by the Bowles attachment

## HEART SOUNDS AND MURMURS

In cardiac auscultation it is important to record the rate rhythm, character and intensity of the heart sounds and the quality area of distribution and the place in the cardiac cycle of any murmurs present Two sounds are normally heard over the heart area The first sound is louder and lower in pitch than the second sound Over the base (aortic and pulmonary areas) the second sound is louder and higher in pitch than the first The aortic second sound in adults usually equals the pulmonic second sound in intensity The closure of the tricuspid and mitral valves and the contraction of the ventricular muscle are the two elements that combine to make up the first heart sound The second sound is produced by the closure of the aortic and pulmonic valves at the end of cardiac systole

**The first sound** of the heart at the apex is normally accentuated after exercise and during fever Abnormal accentuation, however may accompany mitral stenosis, effort syndrome thyrotoxicosis and the paroxysmal tachycardias

Decrease in intensity of the first sound of the heart may be normal in the presence of obesity and emphysema Decrease from day to day may occur if there is an accumulating pericardial effusion or it may accompany infarction of a large section of the cardiac wall In peripheral circulatory collapse where there is a diminished venous return to the heart (shock hemorrhage) decrease in the intensity of the heart sounds may be noted Variations in the intensity of the heart sounds takes place in the cardiac arrhythmias (premature beats heart block auricular fibrillation)

**The aortic second sound** is louder than the pulmonic second sound in individuals over 60 but hypertension in the systemic circulation may cause this accentuation to occur at any age Degenerative changes in the aortic valve (arteriosclerosis and syphilis) may sometimes change the character of the aortic second sound in the absence of hypertension

Aortic and mitral stenosis by decreasing the amount of blood ejected into the aorta at each systole may be accompanied by diminution of the aortic second sound Disease of the valve cusps preventing proper closure may be another factor while sudden left ventricular failure produces the same effect Premature beats may have just sufficient force to open the valves in which event the amount of blood received by the aorta is small and the aortic second sound is weak Many premature beats do not open the pulmonic and aortic valves at all consequently the second sound is

absent In hypotension in certain anemias in prolonged fevers, or following peripheral failure there may be a diminution of the aortic second sound

**Accentuation of the pulmonic second sound** indicates increase in the pressure in the lesser or pulmonic circuit This may be secondary to a left ventricular failure or mechanical defect of the mitral valves, or it may point to a pulmonary hypertension that is seen in some conditions for example tuberculosis emphysema or pulmonary sclerosis that are fore runners of a right sided heart failure

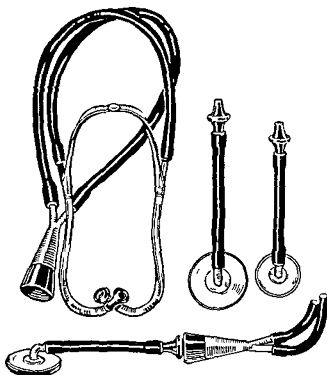


Fig 5 Pilling Bowles combination stethoscope with diaphragm and Ford chest pieces

A diminished pulmonic second sound may be a danger signal of a failing right heart Likewise in the presence of an active stenosing process in the pulmonary valve leaflets the pulmonic second sound may gradually diminish until it disappears Additional signs over this area that should be searched for to confirm this impression are a rough systolic murmur and a palpable thrill

**Splitting of the heart sounds** occurs in health, many times it is related to respiration Splitting of the first heart sound likewise occurs in patients suffering from heart disease for example in intraventricular or bundle-branch block where the ventricles receive their impulses at different times and consequently contract asynchronously (page 623) A splitting of

the second sound at the base of the heart is more common and is caused by asynchronous closure of the aortic and pulmonary valves It may be present normally during certain phases of respiration or it may follow bundle branch block or premature ventricular beat It may accompany either pulmonic or systemic hypertension

**Gallop** In children and young adults a third heart sound may be heard between the apex beat and the left sternal border in the fifth interspace This is a normal finding but at times it may be impossible by auscultation to differentiate it from the extra sound that makes up a gallop rhythm In some cases the clinical findings serve to make the distinction

The term gallop applied to this finding is a good one and should be retained because of its resemblance, especially when the heart rate is above 100 to the sound of the hoof beats of a galloping horse Potain originally described three varieties of gallop rhythm protodiastolic (early diastolic), mesodiastolic and the presystolic (late diastolic) Clinically only two types are important The more common presystolic type presumably is caused by an audible auricular contraction and never occurs in its absence The protodiastolic gallop is a sound that occurs approximately 0 12 to 0 20 second after the beginning of the second sound (Wolferth and Margolies) Gallop sounds are heard best with the patient recumbent and are variable appearing at one examination only to be absent at the next They are altered in the position they occupy in the cardiac cycle and in intensity by changes in the cardiac rate [38] It is well worth while to study these sounds for they often appear with cardiac failure to disappear again as the patient improves following successful therapy They may be produced by either right or left sided failure and are supposedly the result of heightened intra auricular pressure causing the onrushing blood in diastole to strike the weakened ventricular wall with more than the usual force

**Precordial Friction Sounds** The recognition of precordial friction sounds may be helpful in diagnosis and therapy The appearance of a precordial friction rub early in the course of some cases of rheumatic infection may be important in differential diagnosis Friction rubs appearing in patients of older age groups following episodes of chest pain suggest anterior coronary occlusion The pericardial friction is produced by an area of acute pericarditis and is usually a harsh leathery to-and fro sound that coincides with the heart sound and in consequence is independent of respiratory movements In some instances the friction rub may occupy systole alone in which event it may be difficult to distinguish from a murmur However friction rubs change from day to day They likewise may alter their character with firmer pressure of the stethoscope bell or with change in position of the patient On auscultation their point of origin seems to be nearer the ear than the underlying heart sounds which at times are blotted out by the loudness and harshness of the friction

**Clinical Significance of Murmurs** Laennec who was first to describe cardiac murmurs in 1819 believed that they were always produced by organic change in the valve leaflets Later at autopsies he observed normal

valves in patients who had loud murmurs during life This caused him to take the opposite view and he stated that murmurs were of no value in diagnosis Cardiac murmurs may prove to be just as confusing to the physician of today if more attention is focused on them and less on the patient as a whole Murmurs comprise only one feature of the examination and should always be interpreted in the light of other findings The presence of murmurs does not always mean heart disease For example if a loud systolic murmur heard over the pulmonary area in recumbency in a young person is the only finding on physical examination and if it dis appears or becomes less intense when the patient assumes the upright position no heart disease is present No treatment for the heart is needed If the patient has been previously informed about the finding and the word ' murmur has become fixed in his mind the task to convince him that he has a normal heart is not an easy one Many women during pregnancy develop systolic pulmonary murmurs that should occasion no alarm concerning the integrity of the cardiovascular system since they *usually disappear following delivery Systolic murmurs at the apex in the* absence of cardiac enlargement or previous history of rheumatic infection may be viewed in a similar light

Timing Murmurs are either systolic or diastolic in time It is a matter of primary importance to establish their place in the cardiac cycle other wise errors in diagnosis are apt to occur Many physicians as a result of long experience never have to give much thought to the timing of murmurs Mitral stenosis for example is recognized as soon as heard by its char acteristic low pitched presystolic rumble In similar manner we learn to know which dog in the neighborhood is keeping us awake at night by the pitch and other qualities of the bark Experienced examiners often depend on the rhythm of the heart to time the murmur However in the presence of an arrhythmia or with rapid pulse rates this method may fail It is far safer to time the murmur by watching or palpating the apex beat or the carotid artery Riesman was the first to point out a very useful method for timing accurately an apical murmur this method he referred to as transdigital auscultation [313] I have found his suggestion helpful in teaching undergraduates to time murmurs during their first days on the medical wards The following description of the method has been furnished by Dr Riesman

> It is necessary to employ a diaphragm stethoscope and not one of the bell type The index or middle finger is flexed at a right angle and its tip is placed directly over the apex beat. The stetho scope is then laid on the horizontal phalanx of the flexed finger at the angle (Fig 6) It will be found that murmurs may be heard nearly as well through the finger as when the stethoscope is placed directly on the chest and since auscultation and palpation are performed at the same place it is obvious that one can tell readily whether a murmur occurs before the finger is lifted, synchronously

with the lifting or afterward The method also serves well for eliciting the Duroziez murmur in cases of aortic insufficiency This murmur really a double murmur, is heard in the femoral artery when pressure is made on it with a stethoscope just below Poupart s ligament Sometimes the pressure is distinctly painful at others the stethoscope disk is too large for making satisfactory compression If the artery is not properly compressed only one sound is heard By transdigital auscultation, the drawbacks just cited are obviated the to and fro murmur can be readily brought out by regulated pressure with the tip of the finger

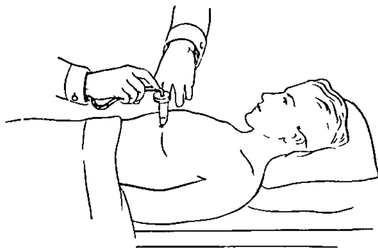


Fig 6 Transdigital auscultation

A murmur is systolic when it occurs between the beginning of the first sound and the beginning of the second, and it is diastolic if it occurs in the longer pause between the second sound and the succeeding first sound A murmur heard in late diastole and continuing up to the succeeding first sound is spoken of as presystolic The heart sound may be replaced by a murmur or both heart sound and murmur may be heard Diastolic murmurs are more serious than systolic murmurs and short murmurs heard with difficulty may be much more important in indicating serious cardiac disease than long and loud murmurs that are readily detected For example the earliest murmur that appears in mitral stenosis is a very short mid diastolic type that often is heard only after exercise with the patient lying on the left side The earliest sign in aortic regurgitation may be a very faint diastolic murmur heard in the aortic area or along the left sternal border

**Determining Site of Origin** It is important to determine the valve area where the murmur has its greatest intensity Murmurs having their

origin in the mitral valve are best heard in the region of the apex beat murmurs arising from the pulmonary valve over the second interspace to the left of the sternum while those having their origin in the aortic valve are heard over the second interspace to the right of the sternum In the latter instance an exception to this rule should be noted In some cases of rheumatic aortic regurgitation especially in children the diastolic murmur is heard best along the left sternal border and may appear to be most intense over the third or fourth interspace close to the sternum

Where a murmur is heard with equal intensity over two areas it may be hard to determine its exact point of origin However if the murmur decreases in intensity as the stethoscope moves away from one valve area toward another the murmur probably originates at the first area If on the other hand the murmur, after diminishing again increases in intensity, as another valve area is approached separate murmurs are probably present The likelihood is even greater if the pitch and intensity of the second murmur differ from the one originally heard

The intensity of any murmur is no criterion of the seriousness of the lesion producing it A small amount of regurgitation at the mitral orifice may cause a loud murmur while a more serious leak may produce a murmur quite difficult to detect or no murmur may be heard at all At times in patients under constant observation if a change can be demonstrated in the quality of the murmur from day to day this may indicate the progression of a lesion of the valvular structure for example, the growth of vegetations in subacute bacterial endocarditis

It is well to adopt some uniform system of terminology in referring to the quality intensity and duration of both heart sounds and murmurs This avoids the use of many indefinite terms that only serve to reveal the uncertainty that exists in the mind of the examiner In Table I the terms in larger type (e g FAINT) are recommended by the American Heart Association for routine use [81] Those in smaller type (e g Weak) are regarded as unsatisfactory (although permissible) synonyms

Some murmurs may be accentuated by exercise and disappear when the patient rests *This is particularly true of the presystolic murmur of early* mitral stenosis Hence a good rule to follow if no murmurs are heard is to auscult again in recumbency after mild exercise Murmurs are better transmitted at the end of expiration when less air is in the lungs In fact faint diastolic aortic murmurs may be detected only at the end of expiration *with the patient leaning forward*

Cardiorespiratory murmurs usually heard over the lung margins should be easily detected for they are always systolic and are always influenced by respiration Harmless or functional murmurs are most common over the second interspace to the left of the sternum In severe anemia and hyperthyroidism systolic functional murmurs are not uncommon

The intensity of any murmur depends upon the velocity of the blood stream at the moment as well as upon the diameter of the valve orifice producing the murmur The intensity determines how far from the heart the

TABLE 1

TERMS TO BE USED IN DESCRIBING HEART SOUNDS AND MURMURS

| INTENSITY | PITCH | QUALITY | DURATION | TIME |
|---|---|---|---|---|
| *Heart Sounds* | | | | |
| NORMAL | | NORMAL | NORMAL | |
| FAINT | | SHARP | SHORT | |
| Weak | | Snapping | | |
| Distant | | Valvular | | |
| Muffled | | | | |
| LOUD | | BOOMING | PROLONGED | |
| Accentuated | | Muscular | | |
| Increased | | | | |
| ABSENT | | SPLIT | | |
| Replaced by | | REDUPLICATED | | |
| a murmur | | RINGING | | |
| | | Metallic | | |
| | | Bell like | | |
| | | Tambour | | |
| | | Hollow | | |
| *Murmurs* | | | | |
| FAINT | HIGH | BLOWING | SHORT | SYSTOLIC |
| Soft | | | | |
| | MEDIUM | HARSH | MODERATE | EARLY SYSTOLIC |
| | | Rough | | |
| | | Coarse | | |
| LOUD | LOW | MUSICAL | LONG | LATE SYSTOLIC |
| | | RUMBLING | | DIASTOLIC |
| | | CRESCENDO | | EARLY DIASTOLIC |
| | | DECRESCENDO | | MID DIASTOLIC |
| | | | | PRESYSTOLIC |
| | | | | (Late Diastolic) |

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murmur may be heard Each murmur usually has a characteristic area of distribution depending upon the nature of the structures that transmit the sound For example the systolic murmur of aortic stenosis is heard in the carotid arteries while the regurgitant murmur often associated with this lesion is heard best along the left sternal border which is the direction taken in diastole by the regurgitant column of blood The murmur of mitral insufficiency is transmitted to the cardiac apex because the structures that transmit the sound come in contact with the chest wall in this area The column of the papillary muscle plays a large part in the transmission of the murmur of mitral regurgitation a fact that can be shown by transplanting the insertion of the papillary muscle of dogs to another portion of the ventricular wall The regurgitant mitral murmur will then be heard best over the new area of insertion

A systolic murmur over the mitral or tricuspid areas occurs in the presence of insufficiency of these valves while a systolic murmur over the pul

monic and aortic valves accompanies stenosis of these orifices Diastolic murmurs are of greater value in diagnosis When heard over the mitral area, they indicate stenosis at the aortic and pulmonic areas, insufficiency It is unwise to make a diagnosis of a valvular lesion based on the murmur alone Search should always be made for other signs that may complete the picture For example, when aortic stenosis is suspected a thrill over the aortic area accompanying the murmur strengthens the diagnosis Likewise the heart should be enlarged and show a characteristic shape on fluoroscopy and the form of the pulse wave will be suggestive When aortic regurgitation is suspected confirming evidence may be present in the peripheral circulation In making the diagnosis of valvular lesions it is also well to remember that lesions of the mitral and aortic valves are much more frequently encountered clinically while lesions of pulmonic and tricuspid valves are rare

**The murmur of patent ductus arteriosus** deserves separate comment It is continuous (both systolic and diastolic in time) and is heard with maximum intensity over the second left intercostal space The pulmonic second sound is often reduplicated is always accentuated and may even in some cases be palpable The murmur of patent ductus arteriosus is transmitted along the pulmonary artery in the direction of the clavicle

**Continuous murmurs** usually with systolic accentuation are likewise heard over other arteriovenous communications (or aneurysms) congenital or acquired A thrill may be palpable over the site of the communication which is usually in the extremities

**The peripheral circulatory signs** that point to an aortic lesion may not be present when the leak is a slight one but occur when the circulation is open and regurgitation free The increased pulse pressure that accompanies aortic regurgitation is visible in patients of medium build in a dancing or throbbing of all arteries most clearly seen in the carotids When it is present to a considerable degree in the suprasternal notch care should be taken not to make the diagnosis of aneurysm The collapsing or Corrigan type of pulse is present in aortic regurgitation the systolic blood pressure is increased and the diastolic pressure is abnormally low (usually 30 to 50 mm ) A capillary pulse may be present and abnormal sounds may be heard on auscultation over the large peripheral arteries (Duroziez s sign—pistol shot sound)

**The diastolic murmurs** most often encountered are the aortic and mitral Little trouble should arise in differentiating them if their characteristic features are kept in mind The aortic diastolic murmur has a high pitch a blowing quality and occurs in early diastole closely following the second heart sound It is usually heard best along the left sternal border when the patient is in the upright position it may be transmitted over a wide area The mitral diastolic murmur on the other hand occurs in mid or late diastole has a very low rumbling or crescendo quality and is heard best in the region of the apex beat with the patient in the left lateral position in recumbency The mitral diastolic murmur is heard over a very

small area in the region of the cardiac apex and unlike the aortic diastolic murmur is separated from the second sound of the heart by a short interval The mitral diastolic murmur is heard best with the bell type of stethoscope while the aortic diastolic murmur is more readily distinguished when the Bowles attachment is used

**Graham Steell Murmur** While aortic and mitral diastolic murmurs nearly always point to the presence of disease valve leaflets on rare occa sions these murmurs may be functional For example dilatation of the aortic ring by hypertension may be accompanied by a short diastolic murmur A similar increase in the pressure in the pulmonary circuit in advanced mitral stenosis may in rare instances be associated with a functional diastolic murmur that can be heard over the pulmonic area This i the Graham Steell murmur Finally in the presence of left ven tricular dilatation either secondary to hypertension or acute rheumatic myocarditis a mid diastolic murmur may be heard over the mitral area simulating mitral stenosis This diastolic murmur may disappear when the myocardium recovers from the severe infection or wnen the acute left ventricular strain is relieved

**Austin Flint Murmur** In some cases of aortic insufficiency the regurgi tant column of blood may float the mitral leaflets into coaptation Conse quently when auricular contraction occurs forcing the blood into the ventricle these leaflets vibrate and a presystolic murmur is heard in the region of the apex This is the Austin Flint murmur When present it may not be easy to differentiate from the diastolic murmur of organic mitral disease However if an apical presystolic thrill is palpable organic mitral stenosis is more apt to be the diagnosis A mall pulse instead of one of the Corrigan variety likewise suggests a mitral lesion

For recording the signs elicited at the different valve areas I have used the system recommended by Segall[335] This graphic method will be employed in some of the subsequent case records to avoid long descriptions Study of Fig 7 will enable the reader to become familiar with these symbols and their meanings

**Amplification Mechanisms** Until recently the unaided senses have been the only means of diagnosis of heart disease at the bedside Constant practice makes the ear of the clinician keen in its analysis of the heart sounds His skill however has natural limitations for he can only inter pret those sounds that fall within the range of perception of the human ear Again the range may be variable since sounds clearly heard by one examiner may not be appreciated by another Experience and practice serve to widen the range of sound perception within certain limits beyond which man must depend on mechanical and electrical aids Both of these have been used to advantage by the research worker in extending our knowledge of cardiac sounds

During recent years rapid strides have been made following the per fection of amplification systems Electrical stetho copes have been intro- duced for teaching purposes and frequency filters have been improved suf

ficiently to eliminate a variety of background noises Today it is possible to pick up the heart sounds in a microphone applied over the cardiac area

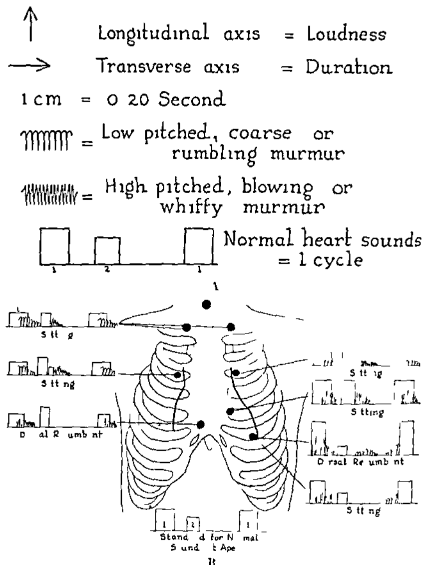



FIG 7 A Code of symbols and rules for the graphic description of cardiac sounds and murmurs Redrawn from Segall *

B The application of the graphic method Reproduction of the record of the signs recorded in a patient with aortic stenosis and insufficiency and mitral stenosis and insufficiency Redrawn from Segall *

transmit them some distance from the patient, and reproduce them on a loud speaker

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**Recording Heart Sounds** Instruments that enable the physician to record the heart sounds are now on the market The sounds of the heart are converted into electrical pulsations by a microphone of special design These pulsations amplified many times are led into the moving coil of a reflecting galvanometer and result in oscillations of a beam of light which is projected on a strip of film moving at a constant speed Part of the light beam is deflected on a ground glass scale enabling its excursions to be observed while recording Provision is also made for listening to the sounds through an electrical stethoscope (amplified auscultation)

The heart sounds may be recorded separately (stethogram) or may be recorded with the electrocardiogram (see Fig 173) If murmurs are present these will be shown by a roughening of the base line which occurs between the first and second sounds if the murmur is in systole and following the second sound if it is in diastole The patterns of these deflections may in dicate the character of the murmur A murmur of high pitch for example will be recorded by many fine sharp pointed deflections while a murmur of low pitch will be represented by fewer less sharply pointed and more widely separated deflections Thrills crescendo murmurs and other sounds that may be present also appear in the graph

The results of the recording of murmurs by this apparatus have not been as satisfactory as the recording of heart sounds Many difficulties are en countered by the uninitiated that make the method one of doubtful value when used outside the laboratory under varying conditions The analysis of the records is especially difficult when vibrations other then the murmurs are encountered and recorded Considering the rapid strides made in the perfection of this instrument however the elimination of the remaining technical difficulties seems possible in the very near future

Split sounds on the other hand may be more accurately analyzed in some cases by the stethogram than by auscultation alone At times the stethogram will aid the clinician in differentiating between a third heart sound and a diastolic murmur Instead of the electrocardiogram the jugular pulse may be recorded simultaneously with the heart sounds in these rec-ords This is very useful in recognizing the difficult diastolic phases

Cautions in Amplification and Recording The physician in the field who is not in constant contact with research workers who have had experi ence in heart sound recording should be cautious in the purchase of this new sound equipment and in the interpretation of the records obtained Likewise if the modern practitioner tries to acquire a knowledge of the technic of all the newer laboratory methods he will find that he has little time left to maintain or increase his skill in the older methods of physical diagnosis After all the machinery of modern medicine is only an aid to our special senses and can never entirely replace them at the bedside We learn the nature of certain puzzling signs through the use of special ized instruments and if we are alert profit by this experience Conse quently the more often we use them the better equipped we become to arrive at correct diagnoses unaided

Careful attention should be paid to the lungs in the examination of every cardiac patient Rales may appear at the bases in beginning congestive failure Pulmonary congestion on the other hand may occur suddenly and be accompanied by cough, frothy, blood tinged sputum dyspnea and cyanosis Numerous fine rales may be heard all over the chest, and these may quickly develop into coarse bubbling rales if fluid continues to be poured out into the pulmonary alveoli

Infarction of the lung following occlusion of the branches of the pulmonary artery by an embolus or thrombus often complicates heart disease When the infarct is small no signs or symptoms appear where a larger area is involved signs are present depending on the location and size of the vessel that is occluded If the lesion is near the outer lung margin in contact with the chest an impaired percussion note may be demonstrated and a friction rub may be heard over the same area In these cases a few localized rales can usually be detected and the patient may complain of pain at this site A cough productive of bloody sputum and an increase in the dyspnea may direct the attention of the physician to the lung fields Many times however pulmonary embolism and thrombosis are unsuspected and consequently undetected until revealed at necropsy In the course of congestive failure hydrothorax is not uncommon It is usually right sided owing to the greater likelihood of obstruction of the right azygous vein Careful examination of the back of the chest of every cardiac patient particularly those showing an increase in dyspnea, is important so that large pleural collections will not be missed

**In the examination of the abdomen** of the cardiac patient the upper right quadrant is first carefully palpated for hepatic enlargement Pain in this area may be the presenting complaint for sudden distention of the liver capsule by congestion causes marked discomfort whereas if the increase in the back pressure is gradual no symptoms may appear Pulsation of the liver accompanies tricuspid regurgitation and is rare Accumulation of fluid in the abdomen occurs in congestive failure (see Fig 2) Ascites may be present early in cases of chronic constrictive pericarditis particularly in children (page 181) The spleen is enlarged in subacute bacterial endocarditis and is a valuable finding to add to the record where a differential diagnosis is sought between this disease and a recurrence of rheumatic infection Abdominal pulsations are common especially in women but the diagnosis of abdominal aortic aneurysm requires the palpation of a definite mass showing expansile pulsation (page 485)

**Examination of the extremities** will furnish valuable data Pulse differences should always be searched for Clubbing of the fingers and toes may occur in subacute bacterial endocarditis When associated with cyanosis clubbing usually points to a diagnosis of congenital heart disease (see Fig 124) The elbows ankles, wrists and knees should be carefully inspected for evidence of rheumatic nodules (see Fig 54) The appearance of these small subcutaneous nodes often aids in the diagnosis of the rheumatic state All reflexes should be tested Signs pointing to a syphilitic

infection of the nervous system may throw light on the nature of an aortic lesion when the etiology is in doubt The legs should be carefully inspected for the presence of edema

## ROENTGEN METHODS IN DIAGNOSIS

While a careful history and physical examination followed by the correct evaluation of all symptoms and signs elicited should enable the physician to manage properly and efficiently the majority of cardiac patients whenever possible at the end of the clinical examination when diagnostic impressions have been recorded a roentgen study should be made[370] This extends the power of inspection a little deeper and comprises the last part of the physical examination of the cardiac patient It may only confirm the diagnosis However in doubtful cases especially where the difficulties of physical examination have been increased by such conditions as obesity emphysema or pregnancy, the roentgen examination furnishes additional information of great value

Before any drawings of the heart outline (orthodiagrams) or roentgen films of the chest (roentgenograms) are made a great deal of information concerning the heart and great vessels can be obtained by fluoroscopy The size and shape of the heart can be seen at a glance By turning the patient in various positions all the cardiac chambers may be studied and their pulsations noted The pulmonary fields are open to inspection and engorgement can be detected while the size density and course of the aorta can be determined Today all of this data is added to the patient s record by the clinician who has invaded the field of the roentgenologist to the extent of making his own fluoroscopic examinations and orthodiagrams It is therefore possible for the entire cardiac study to be completed before the patient leaves the office

Some clinicians still prefer to take roentgenograms with the patient in various positions and to study these later for abnormalities of cardiac size and shape To be satisfactory for this purpose roentgen films must be taken with the tube at a distance of at least seven feet from the patient's chest. In this way only parallel rays from the tube are used and distortion of the cardiac silhouette is avoided (Fig 8) The nearer the tube is moved to the patient the greater will be the distortion of the cardiac shadow At a distance of seven feet or more the rays from the tube are practically parallel but an exact reproduction of the heart size on the film is not obtained The percentage of error however is negligible and the method is suited for clinical purposes[317]

The orthodiagram on the other hand has many advantages To begin with it is much less expensive The equipment necessary consists of a fluoroscope properly fitted with a few special attachments for making orthodiagrams (Fig 9) and the supplies (parchment tracing paper planimeter copying pencils and slide rule) for making and calculating the orthodiagrams[197] True cardiac size is obtained for here the tube is moved by

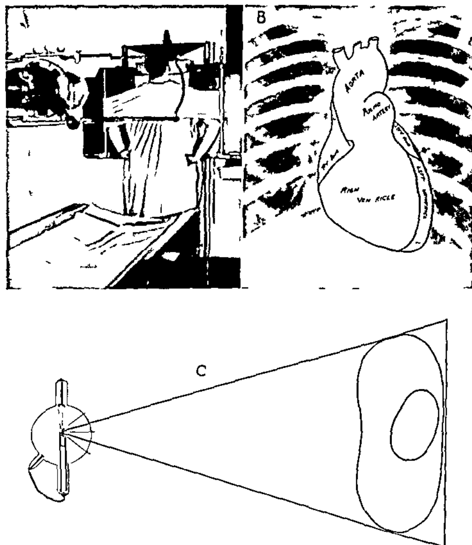



Fig 8 The teleroentgenographic method

A The patient in position with the tube at a distance of seven feet

B The roentgen film The various cardiac chambers are indicated on the silhouette

C Diagram illustrating course of divergent rays It can be seen that the smaller the distance between the tube and the patient the greater will be the distortion on the screen

Advantages of method 1—A standard procedure that can be carried out by a technician 2—This result is more accurate if the orthodiagraphic measurements are made by an inexperienced observer

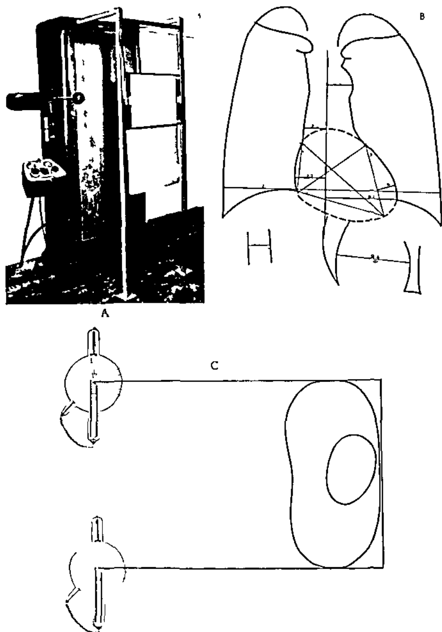



FIG 9 The o thodiagraphic method A Fluoroscope w th orthod agraphic attach ment (Courtesy Westinghouse X Ray Corporat on ) B The orthod agram C Diagram illustrating the p incple of projection Parallel rays are obta ned by moving the tube and no d stortion of the image results

the operator and a small beam of parallel rays, controlled by a shutter, is used to illuminate the cardiac border Experience reduces the incidence of technical errors Finally, it is desirable that the clinician who makes the physical examination should also carry out the roentgen study In this way he can check his findings at once and in addition to determining accurately cardiac size he sees the heart contour in the various positions and can closely study cardiac contractions Valuable data not obtainable at the initial examination may be furnished by a series of studies made on the same patient by the same observer at intervals (see Fig 24)

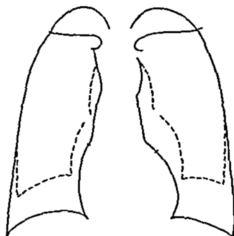


FIG 10 Diagram illustrating the effect of respiration on cardiac position The solid line represents inspiration The broken line represents the position of the heart in expiration

A number of factors influence the size and shape of the normal cardiac silhouette observed during fluoroscopic examination If the respiratory movements are forced distortion of the shadow will result With deep inspiration the heart becomes long and narrow with deep expiration short and broad (Fig 10) The patient should therefore be instructed to breathe normally and slowly In recumbency increase in the return volume of blood entering the heart will slightly widen the shadow, while in the erect position a decrease in the return flow is apt to give a slightly smaller silhouette If the standing position is used all subsequent observations made for purposes of comparison should be carried out in this position

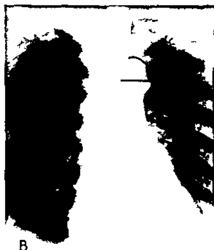
Fluoroscopy may be increased in value if the patient swallows barium paste during the examination This outlines the esophagus and enables its relationship to heart and aorta to be determined (Fig 11)

In every fluoroscopic examination of the heart the patient should be studied in four standard positions

**Anteroposterior Position** In this view the heart appears as a dense shadow in the middle of the chest with the apex directed toward the left




A Displacement of the esophagus by enlargement of the left auricle Patient in the right oblique position




B Kreuzfuchs method for determination of the aortic diameter Patient in antero posterior position (See text)

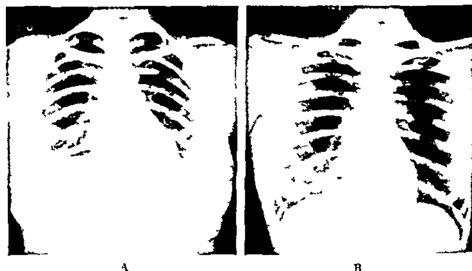



C Right sided aorta Patient in the right oblique position (Courtesy of Dr E P Pendergrass)

FIG 11 The value of the barium filled esophagus in roentgen examinations of the heart and great vessels

Wide variations in cardiac shape may be seen to occur normally, and these will depend upon the body build For example if the diaphragm is high as in individuals of hypersthenic habitus the heart will be elevated and will appear wider (Fig 12A) while in the hyposthenic type the diaphragm is low and the heart assumes a central vertical position (Fig 12B)

In the anteroposterior position the upper curve of the right border (Fig 13) follows closely the right sternal margin and is formed by the great vessels in younger patients the superior vena cava usually occupies



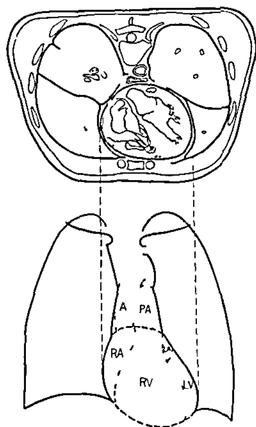
A B

Fig 1 Influence of bodily conformation on the cardiac position and shape
A The hypersthenic type The diaphragm is high
B Hyposthenic type The diaphragm is low (ptotic or drop heart)

this position but in older patients the aorta is seen In the latter instance an arterial type of pulsation is noted in the convex shadow of this region The lower half of the right border curving outward and downward to the cardiophrenic angle is formed by the right auricle Rarely the inferior vena cava and cardiodiaphragmatic ligament become visible below the auricle

Viewing the cardiac silhouette in the anteroposterior position from above downward on the left side the first structure that attracts attention is the aortic knob forming a short curve convex to the left In older patients this may be quite prominent The next small arc seen on the left border varies in its prominence in different patients and is formed by the pulmonary artery It exhibits a lesser degree of arterial pulsation than is usually seen in the aortic area The pulmonary area may be quite convex and prominent in children and young adults but this decreases with advancing years A small portion of the left auricular appendage can usually be seen on the left border inferior to the pulmonary artery Enlargement or

bulging in this region has considerable significance in rheumatic heart disease when mitral stenosis and left auricular enlargement are present The left ventricle constitutes the remainder of the left border amounting to nearly one half of the total length It is usually slightly convex outward and



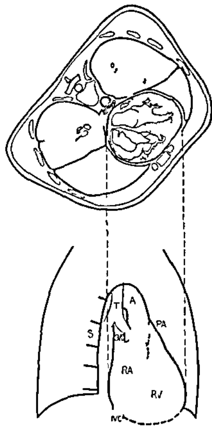




Fig 13 Fig 14

Fig 13 Schematic diagram illustrating topography of the heart and great vessels with the patient in the anteroposterior position

Fig 14 The topography of the heart with the patient in the right oblique position

curves sharply around the apex of the heart At times an air bubble in the stomach may permit visualization of the inferior cardiac border (see Fig 103) but nearly always this part of the outline is lost in the subdiaphragmatic shadows The inferior cardiac border is composed of the left ventricle for a small distance in the region of the apex The right ventricle makes up nearly one half of the remaining distance to the sternum while the right auricle completes the inferior border

**Right Anterior Oblique Position** The examination is continued with the patient in the right anterior oblique position (sometimes called the first oblique or right oblique position) Here the right shoulder remains in touch with the screen while the body is rotated through an angle of approxi

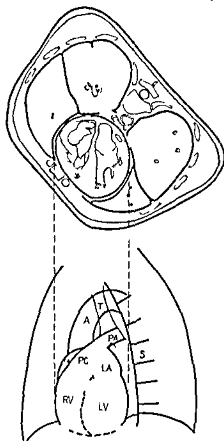



Fig 15

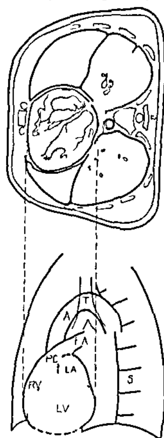



Fig 16

Fig 15 Diagram illustrating the topography of the heart and great vessels with the patient in the left anterior oblique position
Fig 16 Diagram illustrating the topography of the heart and great vessels with the patient in the lateral position

mately 40 degrees (Fig 14) Standard degrees of rotation are unsatisfactory It is best to turn the patient slowly until the cardiac silhouette, as shown in the figure is seen to its fullest extent The right or posterior border of the shadow is now composed of the superior vena cava the right auricle and the inferior vena cava The anterior border is made up of the ascending aorta the pulmonary artery and the right ventricle The right anterior oblique position is most important where early mitral stenosis is suspected The cardiac silhouette in this position will then be altered by the encroachment of the left auricle on the retrocardiac space (see Fig 11)

**Left Anterior Oblique Position** In the left anterior oblique or the second oblique position the patient's left shoulder remains in contact with the screen and he is rotated to the right about 40 degrees This position is particularly suitable for visualization of the aorta The ascending portion can be clearly seen the transverse portion less distinctly, while the descending portion may be followed until it merges with the vertebral column shadow The anterior border of the heart in this position (Fig 15) is formed by the aorta the right auricle and the right ventricle The trachea may be seen at its bifurcation between the ascending aorta and the spinal column This air-containing structure tends to obscure the transverse aortic arch It is important to note that in the left anterior oblique position all the chambers of the heart can be visualized

**Lateral Position** For this view the patient stands at right angles to the screen with the left shoulder forward and both hands behind the head Here the anterior border of the heart (Fig 16) is made up of the aorta and the right ventricle while posteriorly beginning below the arch the border is made up of the pulmonary artery the left auricle the left ventricle and at times a portion of the inferior vena cava The area between the back of the heart and the vertebral column again visualized clearly in this position is the retrocardiac space It is usually clear and normally averages about 2 to 3 cm in width unless the anteroposterior diameter of the chest is small in which event it may be proportionately narrowed or entirely obliterated A careful study of the retrocardiac space with the patient in the oblique position is most essential since both left atrium and left ventricle are posterior chambers and their enlargement may be detected by encroachments upon this area

## Cardiac Size

Cardiac hypertrophy except in a few rare instances means heart disease consequently it is of primary importance to determine the size of the heart While percussion may furnish this evidence roentgen studies are valuable in checking the result and in pointing out the degree of participation of the various cardiac chambers in the enlargement A number of methods for measuring and recording the heart size are in use Of course the first impression as to the presence or absence of cardiac enlargement is gained at the time of the fluoroscopic examination The relationship between the size of the heart and the diameter of the chest is first noted Later this cardiothoracic ratio may be calculated from the roentgen film or orthodiagram To obtain this figure from the orthodiagram drop a perpendicular line of the chest starting midway between the sternoclavicular joints (Fig 17) At right angles to this line draw the transverse diameter of the chest tangent to the dome of the right diaphragm The transverse diameter of the heart is obtained by adding RM (greatest extension of the heart to the right) and LM (greatest extension of the heart to the left) If this figure is divided by the transverse diameter of the chest the result will be the cardiothoracic ratio The normal value is 0 5 but values in

excess of this are not in themselves indicative of cardiac enlargement Alterations in the heart position (Fig 10) and differences in body build (Fig 12) will cause the cardiothoracic ratio to show wide variations

The most valuable criterion in estimating cardiac enlargement is the cardiac area of the orthodiagram In measuring this surface the anteroposterior view must be completed by drawing arbitrary lines to represent

Fig 17 A normal orthodiagram (For explanation see text)

the upper and lower cardiac borders It is then possible to determine the number of square centimeters in the area by the use of a planimeter (Fig 18A) The result can be compared to the predicted value obtained from tables of Hodges and Eyster and the percentage of deviation from the normal noted Early cardiac enlargement may be detected in this manner Normal transverse diameters based on the age height and weight have likewise been estimated and should be included in all cardiac studies A cardiac slide rule made up from the Hodges Eyster formulae (Fig 18B) is available and is useful in quickly obtaining the predicted cardiac area and transverse cardiac diameter of any adult patient

Various diagonals to connect points on the orthodiagram have been

recommended by different workers as a guide to the enlargement of the individual chambers of the heart It is necessary to place certain markings on the cardiac border during the fluoroscopic examination before these diagonals can be drawn (Fig 17) The point (A) on the right cardiac border designates the junction of the superior vena cava and the right auricle (B) the right cardiodiaphragmatic angle (C) on the left border marks the junction of the auricular appendage and the ventricle Incidentally point (C) is not always easy to locate It requires close inspection along the left border during the fluoroscopic study to discern the dividing point or fulcrum where the type of pulsations changes

When these points are marked the orthodiagram is traced from the screen on parchment paper and placed on a drawing board B and C are connected A ruler is placed parallel to the line BC and tangent to the lower end of the cardiac border The point where the border touches the ruler is marked D This approximates the cardiac apex The following lines are now drawn AB this is the chord of the right auricle AD this is the long diameter of the heart A perpendicular line from PP to C(SC) represents the left auricle Other perpendicular lines are drawn from the midline of the chest to the most distant points on each cardiac border (RM and LM) Next connect the points C and D This distance is known as the chord of the left ventricle Now connect B and D This is the chord of the right ventricle A perpendicular from the line CD to the outermost part of the left ventricle is now drawn and marked N This represents the rise of the left ventricle A similar perpendicular from AB to the right auricular border is drawn and marked O This represents the rise of the right auricle To measure the width of the great vessels in the supracardiac shadow perpendicular lines are drawn from the midline of the chest to points of farthest extension to the right (1) and to the left (2) The sum of these should not exceed 7 5 cm but the value will vary depending on age build and amount of tortuosity of the aorta

The aorta may usually be measured in the right and left anterior oblique positions at which time the diameter may be marked on the screen with the patient rotated to the angle giving the greatest visibility and using the smallest possible pencil of parallel rays from the tube In the anteropo terior position the aortic diameter at the beginning of the descending portion may be obtained by using the procedure recommended by Kreuzfuchs This method is based on the anatomic fact that the right side of the descending aorta in the region of the aortic knob parallels the left side of the esophagus As the patient swallows barium paste the left side of the barium column and the left border of the aorta are marked on the screen (Fig 11) From this measurement 3 mm, representing the width of the esophageal wall is deducted

### Characteristic Orthodiagraphic Changes

Certain types of heart disease especially those associated with valvular lesions alter the orthodiagram in a characteristic manner In mitral regurgitation there may occasionally be noted an outward pulsation in the region

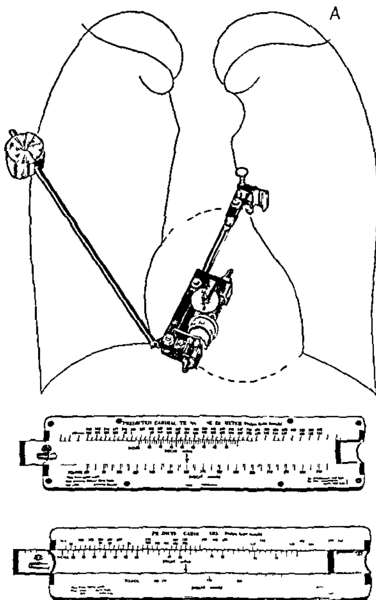



FIG 18 A Calculation of the cardiac area by the use of the planimeter B Th cardia slide rule *

* Manufactured by the Picker X Ray Corporation 300 Fourth Ave N Y

of the left auricle on the left cardiac border occurring during cardiac systole The orthodiagram will show enlargement to the left and downward of the left ventricle (Fig 19)

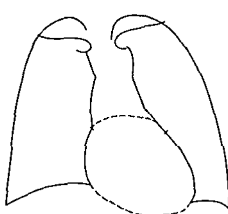


Fig 19 Mitral regurgitation

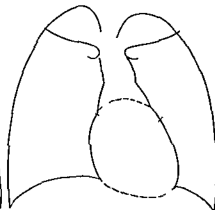


Fig 20 Mitral stenosis

**Mitralization** In mitral stenosis the cardiac silhouette shows characteristic alterations The thin walled left auricle responding to the strain enlarges and the region occupied by this structure on the left cardiac border becomes more conspicuous At the same time increased pressure in the pulmonary circuit causes bulging of the region occupied by the pulmonary artery just above the auricular segment The result (Fig 20) is a straightening of the whole left border of the heart This is spoken of as mitralization The effect is further accentuated by a decrease in the size of the aortic knob

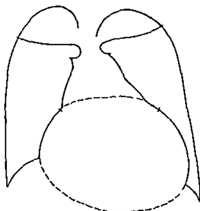


Fig 21 Advanced mitral stenosis and regurgitation

Progress in the mitral lesion tends to reduce the amount of blood entering the left ventricle consequently this chamber does not increase in size—



FIG Advanced mitral stenosis Note the bulge on the right cardiac border caused by the dilatation of the left auricle

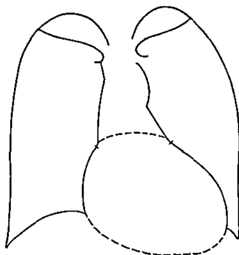
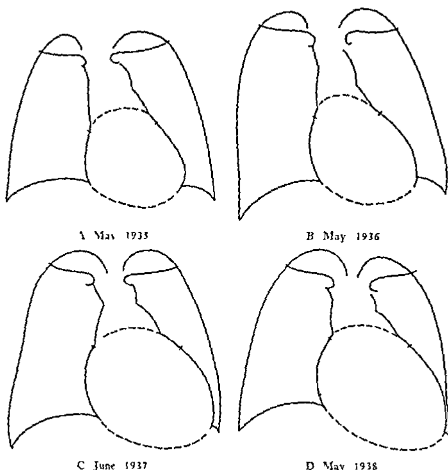


FIG 23 Aortic regurgitation

in some cases even becomes smaller Since both left auricle and left ventricle occupy posterior positions early changes may be detected by turning the patient and noting encroachments on the retrocardiac space in either

the right oblique or lateral views (Fig 11) The enlargement of the left auricle in mitral stenosis may be seen in the upper and middle thirds of the retrocardiac space When there is an accompanying mitral regurgitation with left ventricular enlargement the lower third of the retrocardiac space is likewise narrowed by the increase in size of the left ventricle In



A May 1935 B May 1936

C June 1937 D May 1938

Fig 4 Serial orthodiagrams from a case of rheumatic heart disease with regurgitation and stenosis at mitral and aortic valves Note progressive increase in cardiac size over a period of four years

advanced cases with generalized cardiac hypertrophy the entire retrocardiac space may be obliterated

A greater degree of mitral stenosis and regurgitation causes the heart to assume a triangular shape (Fig 21) This is caused by the combined effect of the two lesions The whole of the left border shows mitralization but in addition there is enlargement of the heart to both right and left

At times in advanced mitral stenosis the left auricle may become so large that it may be seen extending beyond the right cardiac border (Fig 22)

Aortic regurgitation produces left ventricular enlargement (Fig 23) Other conditions such as aortic stenosis and hypertension place a strain on the left ventricle and are accompanied by similar alterations in the cardiac silhouette The aortic knob becomes more prominent and the pulsations in aortic regurgitation will be seen to have an increased excursion In addition to these changes, in patients with syphilitic aortitis and aortic regurgitation the aorta may show considerable increase in density If the



Fig 5 Large pericardial effusion

patient is viewed in the left lateral position the increased size of the ventricle will be indicated by the degree of encroachment on the retrocardiac space In this position the left ventricle occupies the lower two-thirds of the posterior border consequently slight variations in its size may be detected

Combined aortic and mitral lesions alter the cardiac silhouette in proportion to their relative severity Usually all chambers are enlarged (Fig 24) The left ventricular size is always increased and rotation of the patient to the right oblique position shows a marked degree of obliteration of the retrocardiac space by the dilated left auricle

Lesions of the tricuspid valve are rare The clinical diagnosis of tricuspid regurgitation is difficult but fluoroscopically it may be suspected when an unusual degree of pulsation coinciding with ventricular systole is noted along the right auricular border accompanied by pulsation of the superior vena cava Stenosis of the tricuspid valve another rare lesion, will

produce right auricular enlargement with some dilatation in the region of the superior vena cava

Large effusions into the pericardial sac produce a typical alteration of the configuration (Fig 25) This is known as the leather water bottle shape Smaller effusions may be seen in the dependent position of the sac with the patient in the upright position Alterations should be searched for just above the diaphragm where the angle between the liver and the pericardium may become acute In pericarditis with effusion close inspection of the borders of the cardiac silhouette will show decreased pulsations As the fluid accumulates further the pulsations may entirely disappear and the usual cardiac outline may be obliterated Care should be taken not to




FIG 26 Calcium deposits in the aortic valve (Marked by arrow) This patient was a male of 56 who gave a history of several attacks of acute rheumatic infection in childhood A Right anterior oblique position B Left anterior oblique position

mistake the dilated heart with feeble pulsations for this picture of pericardial effusion When in doubt roentgen films taken both in the upright and recumbent positions may be helpful In recumbency it will be noted that the heart becomes globular in shape owing to a more even distribution of the fluid contained within the pericardial sac

Chronic pericarditis should be suspected when the cardiac silhouette is smaller than one would expect to encounter considering the severity of the clinical signs (see Fig 82) In this type of heart a diminution in the pulsation is likewise a characteristic feature

Roentgen films particularly the lateral and oblique views may show calcium deposits and these will be of great assistance in the diagnosis

(Fig 26) Fixation may be demonstrated in chronic mediastinopericarditis by taking roentgenograms in various positions and noting the shift of the cardiac border

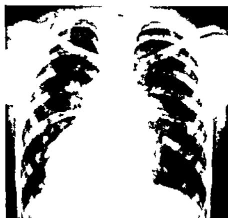




Fig 27 Fig 28

Fig 27 Congenital dextrocardia This patient was a child of 10 who presented in addition the typical signs of an established mitral stenosis Note the cardiac enlargement and mitralization

Fig 28 Patent ductus arteriosus

Congenital cardiac defects occur in a variety of combinations A careful analysis of the contour of the orthodiagram and a consideration of the findings on physical examination will often enable the physician to diagnose correctly the type of congenital abnormality present True congenital dex

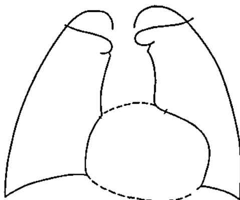


Fig 29 Pulmonary stenosis (Coeur en sabot)

trocardia (Fig 27) presents no difficulty Patent ductus arteriosus in some cases may cause no alteration in the cardiac silhouette If the lumen of the communication is large cardiac size will be increased (Fig 28) and a

prominence will be noted in the region of the pulmonary artery with increased pulsations over this area In stenosis of the pulmonary valve increase in the size of the right ventricle is common This tends to elevate the apex of the left ventricle, producing a cardiac configuration resembling

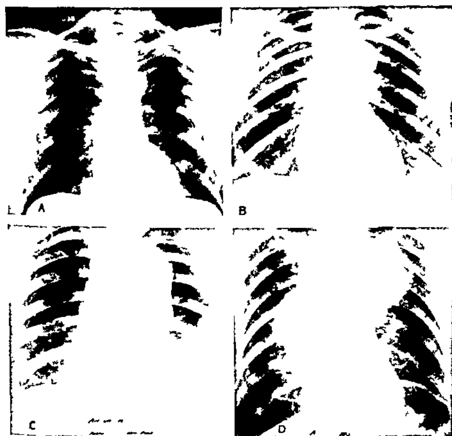



FIG 30 Syphilitic cardiovascular disease
A Early syphilitic aortitis Note the enlargement of the ascending aorta
B Dilated ascending aorta (early aneurysm)
C Aneurysm of the entire aortic arch
D Saccular aneurysms

a wooden shoe the so called coeur en sabot (Figs 29 and 136) In coarctation of the aorta the ascending aorta may be dilated and increased pulsations will be observed The congenital band constricting the aorta increases the work of the left ventricle and hypertrophy of this chamber may result The intercostal arteries serving as collateral pathways in these cases may erode the lower borders of the ribs This change can

usually be demonstrated only by means of a satisfactory roentgen film (see Fig 128)

Measurements of the aorta are occasionally of importance to the clinician in diagnosis In syphilitic aortitis the early changes can be detected only by roentgen examination Experience in the fluoroscopic method increases the ability of the clinician to recognize these differences in aortic density In syphilitic aortitis the aorta may appear on the right cardiac border or the aortic knob may be prominent and the changes in the aortic wall may produce a wider range of pulsations Portions of the aortic wall may weaken early in the process and local bulgings may be seen fluoroscopically long before they can be recognized clinically The aorta should be studied care

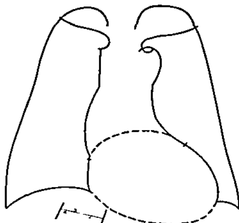


FIG 31 Orthodiagram of a patient suffering from syphilitic cardiovascular disease Aortic regurgitation was present Note aortic dilatation and cardiac enlargement The aortic measurement recorded below was made with the patient in the right anterior *oblique position*

fully in all positions in suspected cases The most common site for aortic aneurysm is in the ascending arch near the base of the heart (Figs 30 and 31) These aneurysms are usually associated with aortic regurgitation and left ventricular enlargement Where the aortic valves are not affected by the syphilitic process and where the mouths of the coronary arteries escape, even large aneurysms may not cause any change in the cardiac size or shape Aneurysms of the transverse arch of the aorta (Fig 32C) by pressure on neighboring structures may cause cough hoarseness or dysphagia Indentation or displacement of the barium filled esophagus by the dilated transverse arch may be readily demonstrated Serial orthodiagrams are useful in following changes in the aorta during treatment

In hypertension the aorta becomes prominent assumes a position on the right cardiac border where increased pulsations can be noted synchronous with ventricular systole At the same time cardiac hypertrophy

FIG 3 Syphilitic cardiovascular disease
A Aneurysm of ascending aorta and innominate
B Fusiform aneurysm descending aorta
C Aneurysm ascending and transverse arches
D Same as C four months later A fatal hemorrhage took place into pleural cavity

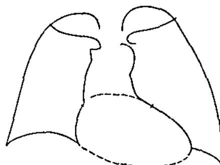


FIG 33 Hypertensive cardiovascular disease

is seen (Fig 33) In the presence of advancing sclerosis of the aorta areas of density corresponding to calcified areas may be detected (Fig 34)

It must be kept in mind at all times that serious heart disease may be present with no alterations in the size or shape of the cardiac silhouette This is true in some cases where coronary sclerosis exists as the single lesion although following occlusion enlargement is quite apt to develop In fluoroscoping all cases that give a history of previous coronary occlusion a close watch should be kept for unusual bulgings in the cardiac outline suggestive of cardiac aneurysms (Figs 35 and 110)

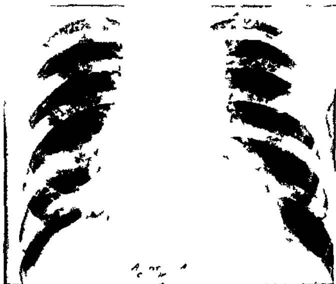


Fig 34 Arteriosclerotic aortitis with calcification

Study of the heart action as a whole during fluoroscopy gives valuable information Auricular contractions precede the ventricular by 0 10 to 0 20 second but this difference can seldom be appreciated by inspection of the silhouette However in cases of heart block auricular contractions may be clearly seen to precede the ventricular contractions The aorta and pulmonary artery are prominent during cardiac systole and stand out distinctly *on the left cardiac border* Exaggeration *of this movement* is seen in some pathologic conditions such as aortic regurgitation and hypertension The whole heart may be seen to have increased excursions in patients suffering from hyperthyroidism However it is important for the beginner to remember that THE CHARACTER AND THE EXTENT OF THE CARDIAC PULSATIONS OBSERVED FLUOROSCOPICALLY SHOULD NEVER BE TAKEN AS AN INDEX OF CARDIAC FUNCTION Weak contractions are encountered in patients suffering from myocardial insufficiency but may also be seen in normal patients who are obese and have high diaphragms with so called transverse hearts

In addition to the roentgen film or teleoroentgenogram and the ortho

diagram another method of study has recently been perfected By means of a grid that moves at a definite rate as exposures are made shadows are obtained that reveal the maximum and *minimum excursions of the cardiac* borders This is known as a kymogram It requires specialized technical

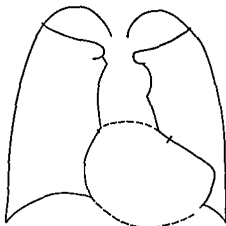


Fig 35 Cardiac aneurysm

methods and is generally employed by those possessing special roentgeno logic training

## ELECTROCARDIOGRAPHY

The electrocardiograph is an outstanding example of the usefulness of the laboratory in clinical medicine Invented and perfected by the com bined efforts of many laboratory workers over the course of half a century it has proved worthy of the high place it holds in medical practice and every physician should possess a knowledge of at least the fundamental principles of the method

The electrocardiogram should always be interpreted in the light of the clinical findings The physical methods of diagnosis properly applied usually yield more abundant evidence than the electrocardiograph for just as the physical examination may be negative in some cases of advanced coronary disease or the neurologic signs produced by some brain tumors *insignificant so the electrocardiogram may be negative in the* presence of such serious conditions as angina pectoris or subacute bacterial endo carditis The graphic method of electrocardiography after all only shows the origin and distribution of the impulse for cardiac contraction It locates accurately an abnormal origin of the impulse and detects the site of any disease process that interferes with its spread but it gives no clue as to the nature of the disease

**Arrhythmias** A knowledge of the cardiac arrhythmias can be very

quickly gained by a study of the alterations they produce in the electrocardiogram In fact, introducing a greater accuracy of diagnosis into the field of the irregularities was an initial task successfully and quickly completed by those working with the electrocardiograph The physician was soon able through the knowledge gained from the study of the electrocardiogram to diagnose unaided nearly all the cardiac irregularities In some instances, the instrumental method must still be called upon to render the final opinion For example if a sinus arrhythmia, a benign condition in itself is accompanied by frequently recurring premature beats or extra systoles the differentiation from auricular fibrillation may be difficult If premature beats alone are observed and diagnosed clinically, it is still desirable to have an electrocardiogram then their point or points of origin may be determined with accuracy If they arise from more than one focus this fact will be shown by the tracing in which event the extra systoles are more apt to accompany organic myocardial disease Furthermore any additional changes that may be encountered in the electrocardiogram may shed more light on the diagnosis

**Infection** When cardiac infection is suspected the electrocardiogram is invaluable In some cases it will furnish the only positive evidence upon which a diagnosis of acute myocarditis can be based For example if an inflammatory process involves the conduction system of the heart delay in the transmission of the contraction impulse may occur At times the impulse may be completely blocked but usually the changes produced in the tracing are slight and transient If these are detected in the absence of cardiac enlargement or other decisive clinical signs the electrocardiogram becomes a valuable aid in establishing the diagnosis and instituting proper therapy

**Paroxysmal rapid heart rates** are often puzzling Although the physician unaided can usually make the correct diagnosis at the bedside the electrocardiogram can be a great help at times For example in paroxysmal tachycardia the electrocardiogram shows whether the paroxysm is of auricular or ventricular origin The ventricular variety is much more serious from the standpoint of prognosis and is more apt to be associated with heart disease The early recognition of the presence of ventricular tachycardia may serve as a warning for it often precedes the onset of ventricular fibrillation The electrocardiogram is also useful in the diagnosis of auricular flutter particularly where high degrees of block are present making an accurate clinical diagnosis difficult

**Essential Hypertension** In the course of essential hypertension evidence of cardiac changes should always be sought in the electrocardiogram If myocardial damage is suggested the regime of treatment should be altered accordingly to lessen the strain on the cardiac reserve

**In angina pectoris** a positive electrocardiogram may be valuable when this diagnosis is in doubt although many times the tracing in angina is negative Electrocardiograms taken during an attack of anginal pain

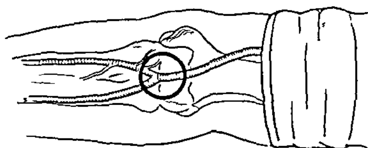
following exercise, or induced anoxemia may show slight alterations in the form of a graph that was previously normal and furnish the necessary objective evidence

**Drug Effects** Drugs alter the appearance of the electrocardiogram As we would expect digitalis produces the most marked and characteristic change and the action of increasing doses is reflected in the rate, rhythm and form of the individual waves Consequently the electrocardiogram is very valuable in giving warning of approaching toxic symptoms that not infrequently occur during the administration of this drug When quinidine is indicated in an attempt to restore normal rhythm in cases of auricular fibrillation and flutter its action can be carefully watched by frequently repeated electrocardiograms

**Valvular Lesions** Occasionally in puzzling cases where valvular lesions are present the electrocardiogram may act as a final court of appeal For example when pulmonary stenosis is suspected the diagnosis is much more likely to be correct if the tracing shows a right axis deviation Aortic stenosis is characterized by a left axis deviation The auricular changes that accompany mitral stenosis often place their mark on the P waves of the electrocardiogram It is readily seen that these various signs may become useful when the clinical signs are inconclusive

**Myocardial Disease** While the earlier field of usefulness of the electrocardiograph was the analysis and classification of the various arrhythmias in recent years the detection of myocardial disease has been its most important function In no other condition is the electrocardiogram as valuable as in coronary thrombosis With the use of the new chest leads the diagnosis of acute myocardial infarction can be made with certainty in over 90 per cent of the cases Occlusion of one of the main coronary arteries or any of its branches produces characteristic changes in the form of the electrocardiogram many times when the remainder of the cardiac examination is entirely negative The alterations that appear are transient and the electrocardiographic picture may change from day to day consequently frequent tracings are necessary in guiding the therapy in any case In spite of the great service rendered by the electrocardiograph in this condition it must be stated that the very small percentage of the cases giving the typical clinical history of coronary thrombosis in which the tracing is negative should always be treated on the basis of the clinical findings

The conclusion can be drawn that the electrocardiographic tracing is a valuable supplement to the examination of every cardiac patient It is an aid in the diagnosis of the arrhythmias a guide to the administration of drugs and reaches its peak of usefulness often when other methods of diagnosis fail in the detection of coronary thrombosis A full discussion of the fundamental principles of electrocardiography and a detailed study of the normal and abnormal electrocardiograms for the reader who is not familiar with the form of these curves will be found in Chapter 24



A

B

FIG 36 Estimation of the arterial blood pressure by the auscultatory method
A Position of the stethoscope in relation to the brachial artery
B The apparatus and technic (Courtesy of the Taylor Instrument Company)

## SPHYGMOMANOMETRY

Most of the models of blood pressure instruments now on the market are satisfactory and are becoming sufficiently rugged in construction to stand the strain of long usage (Fig 36B) Errors under five mm in clinical models that receive ordinary care should not cause alarm More often wide differences in readings are due to the technic used by the observers Recently the committee for the standardization of methods of taking blood pressure readings appointed by the American Heart Association and by the Cardiac Society of Great Britain and Ireland have published suggestions in an attempt to standardize the method of taking and recording the blood pressure readings[3 1] These suggestions summarized below should be given careful consideration by every practicing physician *

1 The equipment should be kept in good condition and calibrated at yearly intervals

The patient should be comfortably seated with the arm free of constriction and supported at heart level on a smooth surface If the readings are taken in any other position notation should be made

3 A standard cuff with rubber bag 1 to 13 cm in width should be used The rubber bag should be applied to the inner aspect of the arm one inch above the ante cubital space Neither bulging nor displacement of the cuff should occur on inflation

4 Palpation should always be used to check results The pressure in the cuff should be quickly increased in steps of 10 mm of mercury until the radial pulse ceases, and then allowed to fall rapidly If the radial pulse is felt at a higher level than that at which the auscultatory sound is heard the palpatory reading should be accepted as the systolic pressure otherwise the auscultatory reading should be accepted

5 In making auscultatory readings the stethoscope should be placed over the previously palpated brachial artery in the ante cubital space (Fig 36A) not in contact with the cuff No opening should exist between the lip of the stethoscope and the skin this should be accomplished with the minimum of pressure possible The hand may be pronated or supinated according to the position yielding the clearest brachial pulse sounds

6 To obtain systolic pressure inflate to a pressure about 30 mm above the level at which the radial pulse can be palpated The cuff should then be deflated at a rate of from two to three mm of mercury per second The level at which the first sound regularly appears should be considered the systolic pressure unless as already described the palpatory level is higher in which event the palpatory level should be accepted This should be noted

7 With continued deflation of the cuff the point at which the sounds suddenly become dull and muffled should be known as the diastolic pressure If there is a difference between that point and the level at which the sounds completely disappear the American Committee recommends that the latter reading should be regarded also as the diastolic pressure This should be recorded in the following form RT (or LT) 140/80 70 or 140/70 0 If these two levels are identical the blood pressure should be recorded as follows 140/70 70 The cuff should be completely deflated before a further determination is made The British Committee believes that except in aortic regurgitation it is nearly always possible to decide the point at which the change occurs and this is the only reading that should be recorded

These specific recommendations should be carefully followed Certain minor points likewise deserve consideration Either mercurial or aneroid instruments are capable of

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correct readings if kept in good condition To this end the mercury manometer should be checked for

(1) Level of mercury It should be kept at zero mark

( ) Small air vent at top of glass tube should be kept clear Incorrect readings occur if this is neglected

(3) Instrument should be kept on level surface and on level with observer s eye for correct readings

A yearly calibration for aneroid type of instrument is recommended since a fall or a blow causes inaccuracies due to changes in aneroid diaphragm The needle should stand at zero when the apparatus is completely deflated and should move immediately when inflation begins Manometers which have a stop pin at zero or those with rotatable dial permitting the user to set the zero mark anywhere are not recommended

All valves should be frequently inspected and should function smoothly The entire system should be free of leakage Rubber cuffs should be 12 to 13 cm wide and 23 cm long The cloth covering should be inextensible material so that even pressure is exerted throughout the width of the cuff it should extend as a band 15 cm wide for 60 cm *beyond the edge of the rubber cuff and then taper gradually during the additional* 30 cm The new style of cuff using slide fastener device is acceptable If bulging occurs above and below the band the reading may be inaccurate

A special cuff should be used to record blood pressure of the leg The rubber bag should be 15 cm wide and 30 cm longer than in the case of the armlet (total 120 cm ) For children cuffs of the following widths have been suggested under eight years less than 9 cm under four years less than 6 cm new born less than 2 5 cm The limited work done in this field does not warrant a definite recommendation at this time For blood pressure readings of the thighs the auscultation should be over the popliteal artery with the patient prone

**Physical and Physiologic Factors** Activity alters the blood pressure consequently the patient should rest for a short period if possible before a reading is made Emotion at the time may likewise influence the result therefore the first reading is nearly always higher Later readings on subsequent visits will show the true blood pressure level

The blood pressure varies at different times of the day In important cases the time of the day should be noted and subsequent observations should be made at essentially the same time in the same relationship to meals sleep exercise and other factors If the physician wishes to minimize the sources of error several blood pressure readings should be made and the highest and lowest pressures of the series recorded

The determination of blood pressure in arrhythmias is unsatisfactory When premature contractions are present the higher systolic pressure of the beats that terminate compensatory pauses should be ignored With auricular fibrillation both systolic and diastolic readings should be recorded as being approximate only Alternation of the pulse (pulsus alternans) during blood pressure determinations may indicate left ventricular weakness

When especially careful studies of the blood pressure are to be made the use of basal blood pressure conditions should be considered The preparation should be similar to that used in making basal metabolism tests The basal blood pressure determination should be made from 10 to 12 hours after a previous meal (preferably in the morning) after the patient has rested 30 minutes in a comfortably warm room and is men

tally as well as physically at ease This procedure is most useful in experimental studies when an accurate standard level is desired Objections to its use in ordinary practice are obvious

At the time of the first examination of the patient the blood pressure of both arms should be taken, since the two may be different In the presence of unexplained high pressure in the brachial artery blood pressure in the legs should be estimated for in this manner conditions such as coarctation of the aorta may be detected

Blood pressure readings vary with age but the often quoted rule that the blood pressure should be 100 plus the age gives values that are too high A systolic pressure consistently above 150 mm of mercury should be considered abnormal at any age The systolic blood pressure readings of normal adults usually vary between 90 and 140 mm of mercury

The diastolic blood pressure is normally between 60 and 90 mm of mercury It can only be determined by the auscultatory method is a much more important reading and shows less variation than the systolic When the diastolic reading of a patient is 120 or over on successive visits the prognosis may be considered poor

The pulse pressure is the difference between the systolic and diastolic pressures It varies between 40 and 70 mm of mercury High values (70 to 120 mm ) are found in hypertension and aortic regurgitation Low values occur in aortic stenosis Addison s disease shock and chronic constrictive pericarditis or acute cardiac tamponade from any cause When the pulse pressure varies from beat to beat pulsus alternans may be the cause This is a very important sign that generally points to a poor prognosis However during paroxysmal tachycardias alternation of the pulse does not have the same significance If alternation is observed when the pulse is slow further clinical examination usually reveals other signs of advanced myocardial disease

Blood pressure in females will average 10 mm lower than in males of the same age and build Since sleep causes a fall in the blood pressure the morning readings may be lower than those taken in the evening Respiration and change in position both influence blood pressure to a slight degree

The blood pressure as usually recorded refers to the brachial artery pressure Readings taken at other parts of the body will be found to vary with the size of the vessel and its position Normally the pressure in the femoral artery is greater than the pressure in the brachial The reverse is true in the presence of coarctation of the aorta Changes in outside temperature may affect the blood pressure and the reading may likewise show considerable variation when cold is locally applied This fact has been made use of in the early detection of individuals predisposed to hypertension who usually show an abnormal response in the blood pressure when an extremity is immersed in ice water for a minute (page 298)

The blood pressure may be estimated by the oscillometric method The use of this instrument enables the physician to acquire additional informa

tion in regard to the character of the arteries of the extremities The oscillometer a triangular metal box is fitted with a special cuff containing two rubber bags A dial with a movable needle records the oscillations of the blood vessel wall while a small aneroid manometer registers the blood pressure level at which they appear and disappear The number of spaces covered by the excursion of the needle is charted for each blood pressure level This is known as the oscillometric index

## Venous Pressure

Determination of the venous pressure is not a new procedure Two hundred years ago Hales measured it by connecting a vein directly to a vertical glass manometer tube The amount of attention that has been given to the question of venous pressure in the past decade and the various methods both direct and indirect that have been devised for its determination indicate a renewal of clinical interest in the subject Venous pressure may be measured indirectly by determining the amount of air pressure necessary to collapse a superficial vein or directly by inserting into the vein a needle connected with a manometer The direct method is simpler more accurate and less time-consuming [97] A convenient apparatus (Fig 37A) consists of (1) an 18 gauge needle (2) a special adapter (3) a 20 cc syringe and (4) an upright manometer tube with a 4 mm bore graduated in centimeters It can be readily assembled and the technic of its successful operation is not difficult to learn

Before the venous pressure determination is made the patient should rest in recumbency on an examining table without a pillow for 15 minutes During this time the apparatus may be sterilized in a shallow receptacle in 70 per cent alcohol The patient s arm is prepared in the usual manner with iodine and alcohol and then supported until parallel to an imaginary line in the mid axilla which is approximately the right auricular level A cuff of a blood pressure apparatus is next placed around the upper arm and inflated to 20 mm of mercury to make the arm veins prominent The apparatus is assembled with the needle on one end of the adapter and the syringe on the other The stopcock of the adapter must be kept parallel to the needle (Fig 37B) As the needle enters the vein blood may be drawn into the syringe for the laboratory and the air allowed to escape from the cuff of the blood pressure apparatus The manometer tube is now fitted into the adapter perpendicular to the arm and the stopcock moved to a position where it is parallel to the manometer tube Blood will at once start up the tube When the column has ceased rising the level on the tube is read This is the venous pressure

The venous pressure of normal individuals at rest in recumbency ranges between 4 and 12 mm of water Exercise causes an increased flow of blood to the heart but in the absence of disease the demand is almost immediately met a greater discharge of blood into the arterial system takes place and there is observed only a slight temporary rise in the pressure If advanced heart disease is present, there is a high venous

pressure reading after exercise which if sustained is indicative of impending cardiac failure Departure from the normal venous pressure readings on slight exertion is seen only in cases where the cardiac involvement is obvious Venous pressure readings will not prove valuable in gauging myocardial capacity in patients in whom congestive failure is absent In other words these readings cannot be used as tests for physical fitness

There is no relationship between venous pressure and arterial pressure

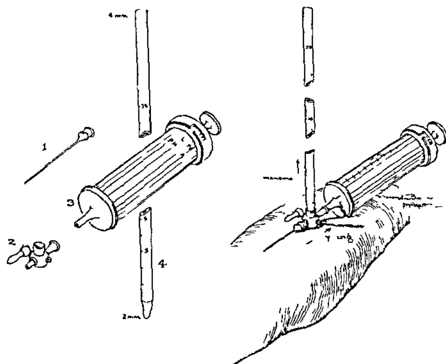



FIG 37 Venous pressure apparatus * A The assembly B Technic of venous pressure determination

in the absence of congestive heart failure The venous pressure readings of 105 compensated cases of hypertension at the Philadelphia General Hospital were found to be within the normal range [97]

Venous pressure estimations are valuable in *diagnosis prognosis and* treatment of heart disease The first sign of beginning congestive failure is elevation of the venous pressure or venous hypertension In the differential diagnosis of allergic and the so-called cardiac' asthma the readings are helpful In pneumonia cases in which the physician is ever on the alert for signs of circulatory failure venous pressure readings are valuable since they can detect an early overloading of the right heart

* Made by the George P Pilling and Son Company Philadelphia

Single venous pressure determinations, like single blood pressure readings, are of little value The venous pressure trend, however, is significant If the curve of the readings shows an increasing venous hypertension, this is evidence of the heart's inability to move the blood from the right to the left side and it precedes edema, cardiac dilatation and reduction of urinary secretion If the venous pressure values show a clear-cut upward trend, little hesitancy should be shown in resorting to venesection in order that the right heart may be at least temporarily relieved of part of its burden Readings consistently over 21 mm of water always indicate the need of venesection After this procedure the benefit may be reflected in the lowered values and if sufficient myocardial reserve is present the heart may respond to the decreased load and the circulation will be carried on with a greater degree of efficiency If in spite of venesection, the signs of congestive failure advance and the curve of the venous pressure readings is upward the prognosis is usually poor On the other hand, if the readings show a steadily downward trend clinical improvement may be predicted Under such circumstances venous pressure is valuable in estimating the myocardial capacity of the patient

An estimate of the venous pressure may be obtained in some cases by inspection of the external jugular veins The height of engorgement in the neck veins with the patient in the erect position serves as a rough guide to the height of the pressure within Normally the veins of the neck are never full in this position In congestive heart failure, they may stand out like cords (Fig 51) In some patients the veins of the neck are difficult to see in which event the veins of the hand may be used Normally these veins are collapsed at the right auricular level so observations made on the distance above this level where collapse takes place give a rough estimate of the extent of the elevation of the venous pressure

## ADDITIONAL LABORATORY AIDS IN DIAGNOSIS

**Urinalysis** In addition to the routine urinalysis, a 24 hour specimen should be collected each day and the amount measured and recorded if the patient is suffering from congestive failure The intake-output charts should be kept until circulatory balance is again restored since they enable the physician to gauge the efficiency of digitalis and diuretic therapy

**Routine blood studies** are essential White blood-cell counts are valuable in estimating the severity and extent of the lesion as well as the progress in rheumatic infection subacute bacterial endocarditis and coronary occlusion Serologic studies for syphilis are most helpful in establishing the etiology in doubtful cases A positive serologic finding almost always indicates that syphilitic infection is present However a positive test does not localize the lesion and hence does not prove that the particular disease complex under consideration is luetic Consequently the clinician must evaluate the positive serology in relationship to the whole clinical picture The incidence of false positive results is 1 per cent

or less when a careful worker employs a standard technic and when the following diseases are excluded infectious mononucleosis leprosy, malaria relapsing fever yaws and trypanosomiasis On the other hand, a negative report does not always exclude syphilitic infection because the sensitivity of the best technics in use today is capable of detecting syphilis in only about 80 to 90 per cent of the cases In other words 10 to 20 per cent of syphilitics will yield false negative serologic reports In the latter group of patients a provocative Wassermann test may be helpful

LOW GRADE CONTINUOUS FEVER Repeated blood cultures should be made whenever a low grade continuous fever is observed particularly in the presence of an old rheumatic lesion A large amount of blood may be required if organisms in the blood stream are few [09] The most common organism isolated from the blood in heart disease is a member of the *Streptococcus viridans* group When a positive blood culture is obtained the finding should be confirmed with one or two additional cultures One patient brought to my attention had 16 positive cultures over a period of several weeks Unless a special study is being made it is preposterous to inflict so many tests on a patient whose prognosis is usually hopeless

BACTERIAL ENDOCARDITIS It is likewise true that many cases of bacterial endocarditis remain undiagnosed because the disease is not suspected A blood culture which often clinches the diagnosis may not be made because the physician hesitates to undertake a procedure which appears to be outside his field In practice however the taking of a blood culture is about as difficult as taking a blood sample for a Wassermann examination or chemical studies The following technic is recommended *

Prepare a tock of 10 per cent solution of sodium citrate place 0 5 cc of the solution in as many flasks as may be need d Plug with cotton; dry and sterlize the containers in a hot air oven at 175 C for one hour and a half This amount of citrate is sufficient to prevent coagulation of amounts of blood up to 20 cc Apply iod ne and then alcohol over the median basilic vein Under aseptic precautions remove 10 to 15 cc of blood place in the flask and rotate the flask gently to insure uniform d stribution of the anticoagulant The sample is then ready to be s nt to the bacteriological laboratory If the cotton plug is not removed from the citrate flask no contamination will occur for at least two months

**Sedimentation Rate** Many recent studies of the erythrocyte sedimentation rate have demonstrated that this property of the red blood cells is often a valuable guide in the treatment of many forms of cardiac disease [309 4 1] Since the technic is simple it will repay the practitioner to add to his equipment the materials needed for carrying out this test

IN RHEUMATIC CARDITIS the sedimentation rate is increased when activity is present and tends to become normal with improvement [363] It is useful therefore both in diagnosis and in management In coronary occlusion a decrease in the sedimentation rate indicates healing of the infarcted area [340]

* Suggested by Dr S Brandt Rose Chief Division of Bacteriology Philadelphia General Hospital Th s method is used routinely for the taking of over 1500 blood cultures per year In the laboratory 2 cc of blood is placed in melted agar and a pour plate is made The remainder of the blood s placed in broth

In these cases the test should be considered along with other factors as a guide to the period of bed rest prescribed

IN SYPHILITIC HEART DISEASE the sedimentation rate is increased and returns to normal following specific treatment In patients who have aortic regurgitation of questionable origin the test may be of value For example at times we are unable to differentiate clinically between an old rheumatic lesion arteriosclerosis and syphilitic aortitis when aortic regurgitation is noted as the single lesion in a patient in middle life The sedimentation rate is normal in the presence of an inactive rheumatic lesion and arteriosclerosis but will be increased in the patient with active syphilitic aortitis Rapid rates may point to a poor prognosis in syphilitic aortitis whereas a decreasing rate during treatment may be viewed as an encouraging sign

CONGENITAL HEART DISEASE if accompanied by cyanosis is associated with an abnormally slow settling time of the red blood cells Normal rates are present in cases showing absence of cyanosis

CONGESTIVE CARDIAC FAILURE During congestive cardiac failure arising from any cause the sedimentation rate is slowed The slowing parallels the failure for when balance is restored the rate returns to normal Pulmonary infarcts speed the rate but if they occur in the course of congestive failure the tendency of the latter condition to slow the rate may balance the mechanism and the result may be a normal figure

**Basal Metabolic Rate** Cardiac symptoms and signs accompany both hyperthyroidism and hypothyroidism When the presence of either is suspected a determination of the basal metabolic rate is indicated This is accomplished by a determination of the rate of oxygen consumption Ordinary activity increases the amount of oxygen utilized by the tissues, consequently the patient must be at complete rest for an hour before the determination is made The test is usually carried out in the morning before breakfast since food increases the metabolic rate and gives a false reading The room where the test is made should be comfortable If it is too hot or too cold the rate will be altered

A variety of small portable machines for determining the basal metabolic rate are on the market today Most of them can be relied upon to give satisfactory results if care and tact are used in the preparation of the patient and if ordinary skill is employed by the technician in charge of the apparatus

The basal metabolic rate is an index of thyroid activity When the reading is plus it indicates overactivity while a minus figure indicates underactivity The figure may show considerable variation although over 90 per cent of normal individuals have a basal metabolism between minus 10 and plus 10

DEPRESSION OF THE BASAL METABOLIC RATE Readings from minus 10 to minus 20 are usually associated with deficiency of thyroid secretion Myxedema states are accompanied by figures from minus 20 to minus 40 per cent Here the clinical picture is typical and in addition the blood cholesterol will be found to be increased (page 373)

ELEVATION OF THE BASAL METABOLIC RATE should be interpreted with care Excitement emotion digestion and fever may give a sizable increase in the absence of thyroid dysfunction In young people with thyrotoxicosis rates as high as plus 70 per cent may be obtained These are usually quickly lowered by rest and iodine (page 357) Essential hypertension or any neurologic condition associated with spasticity or tremor is apt to cause increase in the metabolic rate and care should be used in the interpretation of the readings in these patients Likewise pernicious anemia and leukemia may increase the rate and these diseases although relatively rare should always be ruled out Congestive failure produces an elevation in the basal metabolic rate that according to Harrison [149] is secondary to the labored breathing associated with the dyspnea

Estimation of the basal metabolic rate to be of any value in the diagnosis of thyrotoxicosis should be made by a skilled technician who uses dependable equipment and follows the above mentioned rules More than one initial determination should be made in each case When frequent determinations are impossible in following the progress of a patient the basal pulse rate may be used as a guide to the metabolic rate until the test is made When the patient is at complete bed rest and the pulse rate is 80 or below there is seldom present any great increase in the metabolic rate Basal pulse rates over 100 are usually associated with elevation of the basal metabolism Read s formula in these cases may be helpful B M R = 0 683 [pulse rate + 0 9 (pulse pressure)] − 71 5 For example if the pulse is 100 and the pulse pressure 60 the B M R would be 0 683 (100 plus 0 9 (60)) minus 71 5 equals plus 34 per cent

## NOMENCLATURE OF THE AMERICAN HEART ASSOCIATION

In order that advances may be made in the study of any disease it is essential that workers in various parts of the country use the same terms in designating the same conditions After establishing this uniformity in nomenclature suitable criteria should be adopted for each entity To meet this need the Committee on Cardiac Clinics of the Association for the Prevention and Relief of Heart Disease the predecessor of the Heart Committee of the New York Tuberculosis and Health Association in 1923 prepared a nomenclature covering the diseases of the heart and blood vessels which was introduced into various clinics With certain changes this nomenclature was adopted by the American Heart Association and since this time has been used with success in all parts of the country

Later another committee appointed by the Heart Committee drew up and published an extremely practical guide containing all the criteria for the diagnosis of heart disease Revisions in 1932 and 1939 have increased the usefulness of this small volume * Its contents should be familiar to every physician who undertakes the treatment of cardiac patients

* Heart Disease Distributed by the American Heart Association 50 West 50th Street New York N Y

A glance at the most recent edition will show that the diseases of the heart are considered to include not only the structural changes found in the heart, pericardium and the adjacent structures but also disturbances of function As a result, this broader definition of disease brings within the scope of the nomenclature a number of disturbances that formerly had to be dismissed as functional even though their consequences might have been definitely disabling The usefulness of the nomenclature is increased by this change

The completed diagnosis of every cardiac patient should include one or more titles from each of the main headings of this nomenclature (page 66) There is first a statement concerning the etiology of the disease If structural changes are discovered these should be named or it should be stated that there is no structural alteration Under Part C the cardiac mechanism and any disturbances of cardiac physiology present are included A diagnosis of the cardiac functional capacity and a statement of the patient s therapeutic classification complete the list It is obvious that this comprehensive diagnosis depends on a careful consideration of every aspect of each case and affords a sound basis for management

Certain patients may have symptoms or abnormal physical signs and yet it may not be possible to make a diagnosis of structural disease or any disturbance of cardiac physiology These patients should be re examined at some future date At the time of the examination they are listed as Possible Heart Disease Patients who have no structural defects or physiologic disturbances of the heart but who have another disease capable of causing heart disease may be retained for further observation with the diagnosis of Potential Heart Disease and a statement of the possible etiologic factor

ETIOLOGIC DIAGNOSIS*

1 Anemia
2 Arteriosclerosis
3 Bacterial infection (specify if possible) [1]
4 Congenital anomaly
5 Effort syndrome (neurocirculatory asthenia)
6 Hypertension
7 Hyperthyroidism [1]
8 Hypothyroidism
9 Neoplasm
10 Other etiologic factor (to be specified)
11 Psychoneurosis
*12 Pulmonary disease (to be specified)*
13 Reflex action
14 Rheumatic fever [1]
15 Syphilis [1]
16 Thoracic deformity
17 Toxic agent (specify if possible)
18 Trauma
*19 Unknown*

[1] When one of these diagnoses is made it should be stated if possible whether the etiologic factor is still active or inactive

* Reprinted by permission of N Y Tuberculosis and Health Ass n

## ANATOMIC DIAGNOSIS

### Diseases of Aorta and Pulmonary Arteries

1 Aneurysm (specify location)
Aortitis
3 Arteriosclerosis of aorta
a Without dilatation
b With dilatation
4 Arteriosclerosis of pulmonary arteries
5 Congenital anomaly (specify if possible)
6 Embolism of pulmonary arteries
7 Injury of (specify location)
8 Other diseases of aorta (specify lesion)
9 Other disease of pulmonary arteries (specify lesion)
10 Rupture (spontaneous)
11 Thrombosis of aorta
1 Thrombosis of pulmonary arteries

### Coronary Arteries

13 Arteriosclerosis of coronary arteries
a With narrowing
b With occlusion
14 *Arteritis of coronary arteries*
15 Congenital anomaly of coronary arteries
16 Embolism of coronary artery
17 Injury of coronary artery (specify character of lesion)
18 Other disease of coronary artery (specify)
19 Periarteritis nodosa of coronary artery
0 Stenosis of coronary ostium
1 Thrombosis of coronary artery

### Diseases of Myocardium

(Including Conduction System and Heart as a Whole)

Aneurysm of heart (specify location)
3 Atrophy of heart
4 Congenital anomaly (specify lesion if possible)
25 Degeneration of myocardium (specify type if possible)
6 Enlargement of heart (chambers involved may be specified)
a Dilatation
b Hypertrophy
7 Fatty infiltration of heart
8 Fibrosis of myocardium
9 Infarction of myocardium
a Recent
*b Healed*
30 Injury of heart (specify character of lesion)
31 Myocarditis active
3 Neoplasm of heart (specify type)
33 No structural disease
34 Other structural disease of heart (specify lesion)
35 Rupture of myocardium (specify location)
36 Thrombosis within heart (specify chamber affected)
*37 Undiagnosed structural disease (specify location if possible)*

### Diseases of Endocardium and Valves

38 Congenital anomaly of endocardium of valves (specify lesion if possible)
39 Endocarditis acute bacterial (specify organism)
40 Endocarditis indeterminate
41 Endocarditis subacute bacterial (endocarditis lenta) (specify organism)
42 Injury of endocardium of valve (specify lesion)
43 Mural endocarditis
44 Mural thrombosis
45 Other structural disease (specify lesion if possible)
46 Rupture of valve (specify valve)
47 Sclerosis of valve (specify valve lesion)
48 Undiagnosed structural disease (specify location if possible)
49 Valvulitis active (specify deformity)
50 Valvulitis inactive (specify deformity)
51 Valvular deformity
  a Aortic insufficiency
  b Aortic stenosis
  c Mitral insufficiency
  d Mitral stenosis
  e Pulmonary insufficiency
  f Pulmonic stenosis
  g Tricuspid insufficiency
  h Tricuspid stenosis
52 Calcification of pericardium
53 Congenital anomaly of pericardium (specify lesion)
54 Hemopericardium
55 Hydropericardium
56 Injury of pericardium (specify character of lesion)
57 Neoplasm of pericardium
58 Pericarditis acute
  a Fibrinous
  b Serofibrinous
  c Suppurative
59 *Pericarditis chronic*
  a Adhesive with constriction
  b Constrictive
60 Pneumopericardium

## PHYSIOLOGIC DIAGNOSIS

### Cardiac Mechanism

1 Arrhythmia (undiagnosed)
2 Auricular fibrillation
  a Paroxysmal
  b Persistent
3 Auricular flutter
  a Paroxysmal
  b Persistent
4 Auriculoventricular block
  a Prolonged conduction time
  b Incomplete
  c Complete
5 Auriculoventricular nodal rhythm (Junctional rhythm)
6 Bundle branch block
7 Other arrhythmias (specify)

8 Paroxysmal tachycardia
  a Auricular
  b Auriculoventricular nodal (Junctional)
  c Ventricular
  d Unknown origin
9 Premature contractions
  a Auricular
  b Auriculoventricular (Junctional) nodal
  c Ventricular
  d Unknown origin
10 Sinus arrest
11 Sinus arrhythmia
12 Sinus bradycardia
13 Sinus rhythm normal
14 Sinus tachycardia
15 Ventricular escape
16 Ventricular fibrillation
17 Wandering pacemaker
18 Valvular incompetence
  a Aortic incompetence
  b Mitral incompetence
  c Pulmonic incompetence
  d Tricuspid incompetence
19 Adams Stokes syndrome
20 Anginal syndrome
21 Cardiac insufficiency
22 Carotid sinus syndrome
23 Pulsus alternans
24 Paroxysmal dyspnea
25 Paroxysmal pulmonary edema

## FUNCTIONAL CLASSIFICATION

At the present time there is no clinical test which will measure accurately the functional capacity of the heart For the purpose of this classification it is to be estimated by appraising the patient s ability to perform physical activity The estimate is only approximate for it is derived largely by inference from the history It represents an expression of opinion concerning the functional capacity of the patient as modified specially by his cardiac disease

The diminution in functional capacity which results from a cardiac disorder may be accompanied by discomfort or signs of impaired circulation or both The extent to which physical activity is curtailed and the severity of the symptoms caused by effort are helpful in estimating the degree of reduction in functional capacity Usually structural changes are present in the heart Occasionally as for instance in certain cases of auricular fibrillation or paroxysmal tachycardia or in certain patients suffering from the anginal syndrome no anatomic lesions can be detected

Functional capacity is usually limited because of (1) cardiac insufficiency (2) the anginal syndrome Other less common causes of limitation are paroxysmal tachycardia and complete heart block Physical signs may

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43 Mural endocarditis
44 Mural thrombosis
45 Other structural disease (specify lesion if possible)
46 Rupture of valve (specify valve)
47 Sclerosis of valve (specify valve lesion)
48 Undiagnosed structural disease (specify location if possible)
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57 Neoplasm of pericardium
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## PHYSIOLOGIC DIAGNOSIS

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   a Paroxysmal
   b Persistent
4 Auriculoventricular block
   a Prolonged conduction time
   b Incomplete
   c Complete
5 Auriculoventricular nodal rhythm (Junctional rhythm)
6 *Bundle branch block*
7 Other arrhythmias (specify)

Class III (formerly II B) PATIENTS WITH CARDIAC DISEASE AND MARKED LIMITATION OF PHYSICAL ACTIVITY They are comfortabl at rest Discomfort in the form of undue fatigue palpitation dyspnea or anginal pain is caused by less than ordinary activity

Class IV (formerly III) PATIENTS WITH CARDIAC DISEASE WHO ARE UNABLE TO CARRY ON ANY PHYSICAL ACTIVITY WITHOUT DISCOMFORT Symptoms of cardiac insufficiency or of the anginal syndrome are present even at rest If any physical activity is undertaken d scomfort is increased

## THERAPEUTIC CLASSIFICATION

The Therapeutic Classification is intended to serve as a guide in the management of patients For each class, it gives a prescription for the amount of physical activity which is advised

The functional capacity of the patient does not always determine the amount of physical activity which is permitted For example a child with active rheumatic carditis may not experience discomfort on playing base ball yet the physician knows that rest in bed is imperative * There is frequently a difference between the amount of physical activity which the patient can undertake in terms of his functional capacity and that which he should attempt in order to prevent further cardiac damage and bring about improvement The recommendation as to physical activity is based upon both the amounts of effort possible without discomfort and the nature and severity of the cardiac disorder

### CLASSIFICATION OF PATIENTS

Class A Patients with card ac disease whose ordinary physical activity need not be restricted

Class B Patients with ca diac disease who e ordinary activity need not be restricted but who should be advised against unusually severe or competitive effort

Class C Patients with cardiac d sease whose ordinary physical activity should be moderately restricted and whose more st enuous hab tual efforts should be discont nued

Class D Patients with cardiac di ease whose ord nary physical activity should be markedly restricted

Class E Pat ents with cardiac d seas who should be at complete rest confined to bed or chair

### POTENTIAL HEART DISEASE†

Patients in whom no cardiac d sease is discovered but whose course should be followed by period c examinations because of the presence or h story of an et ologic factor which might cause hea t d sease The d agnosis in these cases is Potential Heart D sease The etiologic diagnosis should be recorded

* Su h a patient would be cla sified as I E

† There are pat ents in whom the symptoms or s gn though uggestive of cardiac disease do not justify a definite d agnos s and from whom is obt ined a history of an et ologic factor which might caus heart d sease The d agnosis in s ch cases is both P tential Heart Disease and Poss ble Hea t Disease

be present or absent but their presence or absence should not influence the rating

The classification of patients according to their functional capacity is not to be used as a guide to formulating a plan for management A therapeutic program particularly with respect to regulation of physical activity, is based on information derived from many sources and is considered in the section on Therapeutic Classification Functional classification should not be influenced by the character of the structural lesion or by judgment as to prognosis Psychogenic disability is discounted For example cardiac functional capacity is not regarded as seriously limited when it is clear that the patient's incapacity is due to a psychoneurotic state, even though organic heart disease is present

In the estimation of cardiac functional capacity the term "ordinary physical activity' is used to describe the actual performance of which each patient was capable prior to the onset of manifest cardiac disease Such factors as the presence of active infection in the heart other acute infectious diseases convalescence from an illness muscular weakness anemia arthritis and psychogenic disability may interfere with judging accurately the capacity for exercise In cases of cardiac disease dating from early childhood a patient s normal functional capacity cannot be estimated In estimating a patient s response to effort a comparison must be made between his ordinary and his present capacity for physical exertion Usually this estimate is based entirely on the history particularly with reference to the patient s symptoms on effort An accurate account of the reaction produced by varying degrees of exertion such as walking on the level or up a grade ascending stairs or running is an essential part of the history In general the more intense the subjective symptoms the more marked are the physical signs of cardiac insufficiency Discrepancies may exist between the number and intensity of the physical signs and the degree of subjective distress on effort This is apt to be true particularly in patients suffering from the anginal syndrome, in whom objective evidences of disease may be slight or absent

If there is doubt as to the rating by the method described direct observation of a patient on performing exercise may be helpful The occurrence of undue dyspnea and the appearance of cardiac pain are of special significance

## CLASSIFICATION OF PATIENTS

Class I PATIENTS WITH CARDIAC DISEASE AND NO LIMITATION OF PHYSICAL ACTIVITY Ordinary physical activity does not cause discomfort Patients in this class do not have symptoms of cardiac insufficiency nor do they experience anginal pain

Class II (formerly II A) PATIENTS WITH CARDIAC DISEASE AND SLIGHT LIMITATION OF PHYSICAL ACTIVITY They are comfortable at rest If ordinary physical activity is undertaken discomfort results in the form of undue fatigue palpitation dyspnea or anginal pain

the heart There were no symptoms referable to the cardiovascular system The past history was negative for rheumatic infection The family history revealed nothing of importance The exercise tolerance of the patient was excellent

PHYSICAL EXAMINATION revealed the presence of moderate cardiac enlargement which was confirmed by roentgen examination No other evidence pointing to cardiac disease could be elicited The blood pressure weight and the nutritional history showed no departure from the normal The blood Wassermann was negative The blood count and urinalysis were negative The electrocardiogram was normal

CLINICAL DIAGNOSIS A Etiologic Unknown B Anatomic Cardiac hypertrophy C Physiologic Normal sinus rhythm D Functional Classification Class I Therapeutic Classification Class B

# 2

# HEART FAILURE

The foxglove's leaves with caution given
Another proof of favoring Heav'n
Will happily display
The rapid pulse it can abate
The hectic flush can moderate
And blest by Him whose will is fate
May give a lengthen'd day
Withering's *Botany*

## MECHANISMS

The aim of all treatment in heart disease is to prevent or if this is impossible to delay for a considerable period the onset of heart failure The signs and symptoms that point to myocardial weakness may be sudden in onset with congestive manifestations in various parts of the body or they may develop slowly after the functional capacity of the heart has been impaired for a long time In clinical practice heart failure is commonly referred to as 'right sided or left sided indicating that in the beginning at least, the process is chiefly confined to one ventricle This may be better understood when we consider the fact that in some conditions such as hypertension aortic stenosis or regurgitation, or coronary disease with infarction, a continued strain is placed upon the left ventricle Cardiac hypertrophy follows to enable the patient to combat these abnormalities and *it may develop in the absence of symptoms When this response has reached* its maximum and the burden on the heart is unrelieved failure becomes imminent Dilatation of the left ventricle occurs and the blood received from the right ventricle does not all reach the systemic circulation Consequently an engorgement of the pulmonary circulation results If the failure of the left ventricle takes place suddenly the acute engorgement of the lungs may precipitate a paroxysm of cardiac asthma or paroxysmal nocturnal dyspnea The situation then assumes the nature of an emergency, cough develops with expectoration of frothy bloody sputum and is followed by orthopnea If the onset of failure is slow the right ventricle may be able to meet the demand placed upon it by the stagnation of the blood in the lungs by increasing its work In time this chamber likewise shows hypertrophy If failure of the left ventricle occurs gradually dyspnea will increase, and it will appear on less exertion Tachycardia will rarely be absent Examination at this time will reveal an accentuation of the pulmonic second sound giving evidence of the dilemma

present in the lesser circulation If the pulmonic second sound has previously been normal this finding takes on added significance at a follow up examination The systolic apical murmur that accompanies the increase in the pulmonic second sound generally signifies a functional regurgitation through the mitral valve It is of interest of course to note this murmur but it is much more important from the standpoint of management to study the heart sounds and to detect a gallop rhythm at the cardiac apex if it is present Inspiratory rales at the lung bases should be searched for at each examination Another valuable sign of exhaustion of the left ventricle is pulsus alternans which can be demonstrated by the use of the sphygmomanometer (page 53) By this sign early failure of the left ventricle may be revealed and intensive treatment begun

The most common cause of failure of the right ventricle is previous failure of the left side of the heart[2 3] Sooner or later following left ventricular failure that is attended by the symptoms just described the right ventricle dilates and fails in which event the characteristic signs and symptoms of this condition are added to the clinical picture Certain types of heart disease may predispose to failure of the right side of the heart for example mitral stenosis or extensive pulmonary fibrosis where resistance to the blood flow is materially increased (Table II) In these instances after a long

TABLE II

FACTORS PRODUCING STRAIN ON THE HEART

| PRIMARY LEFT VENTRICULAR STRAIN | PRIMARY RIGHT VENTRICULAR STRAIN | PRIMARY STRAIN ON BOTH VENTRICLES |
|---|---|---|
| Arterial hypertension | Mitral stenosis | Mitral insufficiency |
| Aortic stenosis | Pulmonic valve stenosis | Multiple valvular disease (chiefly aortic and mitral) |
| Aortic insufficiency | Pulmonic valve insufficiency | Severe anemia |
| Infarction of the left ventricle | Pulmonary endarteritis | Arterial hypertension aortic valve disease or myocardial infarction *plus* factors producing right ventricular strain |
| | Organic tricuspid insufficiency | |
| | Marked pulmonary fibrosis | |
| | Marked pulmonary emphysema | |

| PRIMARY STRAIN ON LEFT VENTRICLE AND SECONDARY STRAIN ON RIGHT VENTRICLE |
|---|
| Factors listed in the first column above plus failure of the left ventricle |

(After Thompson and White)
Reprinted by permission C V Mosby Co Amer Heart Jou 12 643 (December) 1936

continued strain the time arrives when the blood cannot be efficiently pumped through the lungs There is a damming back into the right auricle with functional regurgitation at the tricuspid orifice and signs of right ventricular failure quickly appear The liver at first bears the major part of the burden and accommodates all the excess blood that is possible In cases where the failure occurs suddenly there is acute liver engorgement the capsule is stretched and pain is usually present under the right costal margin If the stasis takes place gradually the liver enlargement may occur without local pain or tenderness but the other signs of venous engorgement will be apparent in the cord like neck veins (Fig 51) If failure is unrelieved effusions follow with the production of hydrothorax and ascites (See Fig 2) Renal stasis may cause oliguria and albuminuria

While it is valuable whenever possible to consider right and left ventricular failure separately there are instances when both sides fail together An example of this is seen in the sudden appearance of signs of congestion that sometimes accompany the paroxysms of tachycardia or fibrillation which occur in the badly damaged hearts of older people The patients with advanced signs of congestion who are seen by the physician in emergencies often present a picture of the late combination of both types Owing to the predominance in practice of the factors contributing to left ventricular failure (high blood pressure and coronary artery disease) this form is much more apt to be encountered than right sided failure

*There have been two schools of thought concerning the mechanisms be*hind the phenomena of congestive failure The first or back pressure theory I have just reviewed Stokes[3 3] and later Mackenzie were proponents of the forward failure theory Mackenzie [0] stated that dropsy was due to diminution in the force that propels the blood through the capillaries all the symptoms of heart failure arising because of this impaired blood supply

The recent extensive investigations of Harrison[149] have thrown considerable light on the whole subject of cardiac failure and in my opinion they furnish the necessary proof that the symptoms of congestive failure are not caused by diminished flow to the tissues First of all edema and dyspnea are not usually present in such conditions as shock and hemorrhage which are associated with decreased cardiac output Harrison shows that patients with congestive heart failure have been observed who have normal figures for cardiac output and these figures do not increase when congestion clears Finally he offers in evidence the fact that the therapeutic measures forming the backbone of successful treatment of cardiac failure (venesection digitalis and diuretics) do not cause increase in the output of the heart

## CLASSIFICATION

A better understanding of the various types of cardiac failure and their underlying mechanisms is most essential before therapy can be discussed

The following classification has been proposed by Harrison (Table III)

TABLE III

CIRCULATORY FAILURE

I FORWARD FAILURE

A—Forward Failure of the Peripheral Vascular Apparatus ( shock collapse )
  1—Hematogenic ( secondary shock )
  2—Neurogenic ( primary shock )
  3—Vasogenic
B—Forward Failure of the Heart
  1—Sudden Death (Due to Ventricular Fibrillation)
  2—Cardiac Syncope
    (a) Neurogenic
      Psychogenic— simple syncope
        vasovagal syncope
    (b) Reflex
      Carotid Sinus Syncope
      Vago-vagal Syncope
      Oculo-cardiac Syncope (?)
    (c) Cardiogenic
      Adams-Stokes Syndrome
      Syncopal attacks in patients with lesions of aortic valve
  3—Cardiac Collapse
    (a) Marked tachycardia
      Auricular Flutter
      Auricular Fibrillation
      Auricular Tachycardia
      Ventricular Tachycardia
    (b) Acute severe myocardial injury
      Coronary Thrombosis
      Diphtheritic Myocarditis
    (c) Mechanical hindrance to heart
      Cardiac Tamponade (a sudden accumulation of blood or fluid in the pericardium)
      Massive Pulmonary Embolism
      Ball Valve Thrombus obstructing mitral orifice
      Inversion of mitral leaflet

II BACKWARD FAILURE

A—Failure of the Left Side of the Heart
B—Failure of the Right Side of the Heart
C—Failure of Both Sides of the Heart

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The peripheral circulation may fail under a variety of circumstances acute hemorrhage (hematogenic) reflex or psychic disturbances (neurogenic) or following the action of substances like histamine acetyl choline or adenylic acid directly on the vessels (vasogenic) The symptoms that ensue (termed shock or collapse ) consist of weakness and vertigo that may be followed by syncope and unconsciousness in severe cases fall in body temperature and sweating No dyspnea appears The patient has a grayish color a rapid feeble pulse a decreasing blood pressure and is able to lie flat in bed Inspection will likewise show that the veins of the neck are not engorged

These symptoms may be caused in a variety of ways For example less blood may be returned to the heart owing to a decreasing venous pressure consequently the output of the heart will be reduced A diminished blood

pressure may also result from the vasodilating influences of various substances acting directly on the peripheral vessels or on the controlling mechanism in the central nervous system

It is essential to recognize peripheral failure when it is present and thus avoid prescribing unnecessary treatment for the heart This is all the more important since recent investigations have pointed out that digitalis may actually be a harmful drug in the treatment of peripheral circulatory failure secondary to acute hemorrhage The emergency treatment in peripheral circulatory failure is discussed on page 511

In contrast to the type of 'forward failure that has its origin in the peripheral circulation (*Table III*), the heart itself may be responsible Here we first consider sudden death that may result when ventricular fibrillation occurs Where sudden forward failure takes place and is followed by recovery it is termed cardiac syncope The condition known as 'simple syncope or vaso-vagal syncope is distinguished from the syncope of peripheral failure chiefly by the slowness of the pulse since tachycardia is the rule in peripheral collapse Again venous distention often follows cardiac collapse while the veins are empty in peripheral failure Carotid sinus syncope (page 378) is one of the possible reflex mechanisms, while the vagus may be responsible in other cases (vago-vagal syncope) Oculocardiac reflexes have also been described by Harrison

More serious lesions in the heart itself (cardiogenic) may be responsible for syncope For example the Adams Stokes seizures that appear in cases of A V heart block are considered under this heading The mechanism and treatment of this type of failure have been described elsewhere (page 405) Cardiac failure or collapse may follow the sudden onset of an ectopic rhythm (page 398) When the burden imposed upon the myocardium by one of these abnormal mechanisms is well tolerated by an elderly patient we may be optimistic in regard to the prognosis It is certainly not worth while to perform additional functional tests in such instances

Acute coronary occlusion may be immediately followed by cardiac collapse if a large area of cardiac muscle is suddenly deprived of its blood supply (page 265) In our ward records we often speak of these patients as shocked However the picture differs from that usually encountered in peripheral circulatory failure in the amount of dyspnea or orthopnea that follows occlusion Likewise in many cases of occlusion rales may appear in the lungs and if the patient survives the appearance of venous congestion also verifies the presence of cardiac failure

Mechanical hindrance to the diastolic filling of the heart may occur acutely when blood or exudate accumulates in the pericardial sac (page 164) or it may follow the development of constricting bands of adhesions in which event the cardiac tamponade may be chronic and progressive (page 181) A large pulmonary embolus may likewise act as an obstruction to the blood entering the lungs and arrest heart action (page 425) Large ball valve thrombi may occlude the mitral orifice and cause sudden cardiac collapse (page 152) A rare accident that may be classified under this head

ing of failure from mechanical hindrance to the cardiac action is eversion of the mitral valve (page 265)

This classification of the varieties of forward heart failure as well as the mechanisms responsible should be familiar to every physician It permits so clear an understanding of the many aspects of the problem that it can not help but result in better treatment "Backward failure" (the dyskinetic syndrome or failure of the congestive type) will be considered in the remainder of this chapter

The careful examination of the myocardium at autopsy in cases of "backward failure" generally shows no anatomic change The old term "chronic myocarditis" so often used in referring to patients with congestive failure following hypertensive heart disease, has been discarded owing to the fact that no fibrosis or inflammatory changes can be found Heart failure is purely a functional condition that is produced by exhaustion associated with certain chemical changes in the cardiac muscle fibers These important changes elude the pathologist at post mortem The various conditions that bring about this functional change by the extra burden they impose on the circulation are numerous Included here are long-continued hypertension [illegible] valvular lesions recurrent carditis coronary thrombosis, [illegible] pulmonary fibrosis, congenital defects uncontrolled abnormal rhythms [illegible] effusions into the pericardial sac Environmental or occupational factors are likewise important in producing the evidences of failure at an earlier date in some patients than they appear in others Except in [illegible] overwhelming rheumatic infection or in the presence of marked congenital defects "backward failure" is rarely met in children while [illegible] plicates the course of rheumatic heart disease in young adults There is a marked increase in the incidence of congestive failure in pa[illegible] years of age because of the greater number of etiologic agents [illegible] time that are capable of placing the necessary strain on the [illegible]

Sodeman and Burch[349] in a recent study of the precipitat[illegible] congestive failure in 100 consecutive cases found that a d[illegible] be assessed in 52 9 per cent of the instances In the patients [illegible] care who showed a gradual onset of failure without demonstra[illegible] the prognosis was poor Over 95 per cent of this group failed [illegible] sate sufficiently to undertake minimal activity If a cause was [illegible] removed the prognosis they discovered was much improved [illegible] per cent of these instances there was sufficient strength [illegible] at least minimal activity The etiologic diagnosis was [illegible] cant in only one group of patients—those suffering fr[illegible] disease with aortic regurgitation These patients when [illegible] developed were usually unable to regain their bala[illegible] precipitating cause

Any circumstance that places a transient and a[illegible] the circulatory apparatus may act as a precipitat[illegible] children upper respiratory infections leading to reac[illegible] process are largely to blame Overexertion in any [illegible]

a delicate balance and cause signs of congestion to appear Pregnancy, hemorrhage overeating overindulgence in alcohol or mental shock may likewise act as precipitating causes *In older patients urinary tract in*fections particularly those associated with prostatic obstruction, cause increase in the blood pressure and this may upset the cardiac balance Consequently an attempt should be made in every patient treated for congestive failure to determine the cause of the breakdown Its significance as far as future management is concerned is obvious

**Fever** often accompanies congestive failure In some cases when of slight degree no demonstrable cause may be evident in which event it is customary to attribute the fever to the congestive failure However when the *increase in the temperature is more marked a complication should be sus*pected and confirmatory evidence carefully sought The four most common complications in order of their frequency in a series of cases studied by Kinsey and White[190] were pulmonary infarction pulmonary infection active rheumatic infection and acute coronary thrombosis

## TREATMENT OF CONGESTIVE FAILURE

### General Measures

***Making the Cardiac Patient Comfortable*** *The first indication in the* treatment of congestive failure is to make the patient as comfortable as possible The special bed shown in Fig 38 is ideal but is usually available only for hospital treatment Some supply houses rent these special beds at low figures for patients undergoing treatment at home and at times the problem may be solved in this way If the whole bed is not obtainable, a special spring that fits the bed already in use may be secured

In the absence of special beds the patient can be made more comfortable by discarding the various back rests (usually the canvas type) already in *use and mobilizing the supply of household pillows The large ones are* stacked and one is placed under the knees Smaller softer pillows are convenient for the head and under the elbows If the elbows are protected from the start considerable discomfort will be spared the patient at a later date

When the treatment is carried out at home it will usually be better to use the bedside commode The exertion of getting out of bed to the commode is less than would be expended trying to use the bed pan satisfactorily In an emergency commodes may be constructed easily from an old chair

Large doses of cathartics certainly do not add to the comfort of the patient at the beginning of treatment They are no longer given with the purpose of promoting the loss of large quantities of fluid by bowel for the modern diuretics make this procedure unnecessary Today the patient is fortunate in that he takes his digitalis straight and not mixed with various ingredients of a violent nature The added rest that this affords contributes in no small degree to the chances of recovery Later in the course of treat

ment mild laxatives may be given but it is always well to avoid the effervescent variety Epsom salts in small doses is the cheapest and best of the group and may be given occasionally in the early morning an hour before breakfast

The fact that the patient has been placed in bed with his position properly adjusted does not guarantee complete physical and mental rest Worry emotional excitement and noises will induce a state of continued tension of all the skeletal muscles in many patients Until this is relieved

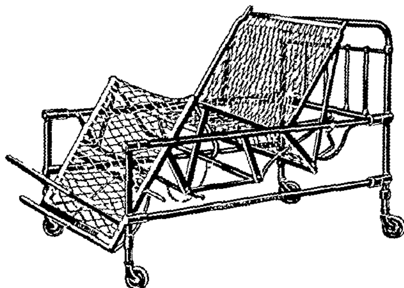


FIG 38 The cardiac bedstead (Redrawn from Diseases of the Heart Sir Thomas Lewis )*

full benefit of any treatment becomes impossible Considerable relief can be gained as Osler stated by the simple process of slowing the body engines While a habit of living cannot be abolished at a command a skillful practitioner soon learns enough about his patient to suggest measures that will result in a greater degree of relaxation

The best drug with which to begin treatment of an attack of congestive failure is morphine A hypodermic injection of 15 mg (¼ grain) as soon as the patient is seen and the diagnosis is established acts like a charm It quiets the patient physically and mentally and should never be withheld unless a marked idiosyncrasy to the drug is known to exist Morphine allays dyspnea as well as restlessness and insomnia and during the calm that follows its administration definite plans may be made for the future care of the patient The dose may be safely repeated for the acute episodes of dyspnea until this symptom is controlled since the danger of drug addic

* Published by permission Macmillan Company N w York

tion from the use of hypodermics of morphine in the presence of congestive failure is slight if ordinary care is used in each case The fear of addiction should not deprive the patient of the relief that this drug quickly brings to the dyspnea and distress that accompany an attack of congestive failure

When balance is restored restlessness and insomnia may be combated by the use of milder sedatives Phenobarbital may be given in 30 mg (½ grain) doses fortified with 0 7 Gm (10 grains) of sodium bromide after meals If there is restlessness only at night one of the more quickly acting drugs such as sodium amytal may be used Chloral hydrate is now recognized as a safe hypnotic and fear of producing cardiac depression by ordinary doses should not prohibit its use

## DIGITALIS

Although digitalis was known as an ingredient of many family recipes for dropsy before the appearance of William Withering's An Account of Foxglove and Some of Its Medicinal Uses in 1785[418] it remained for this country doctor and botanist to provide the first complete scientific study of the drug (frontispiece) It is unfortunate that in the subsequent years his advice regarding the method of administration of digitalis was entirely disregarded and for well over a century a haphazard use of the drug prevailed Paralleling the revival of interest in digitalis in recent years a vast literature has been built up by the contributions of physiologists pharmacologists and clinicians While many of the beneficial effects of this remedy have been satisfactorily described the final story remains to be written

### Action

The modern concepts concerning the mode of action of digitalis should be thoroughly understood by every physician who prescribes the drug Therefore I offer no apology for including a short review of the present-day belief regarding the mechanism of the principal therapeutic and toxic actions the pharmaceutical preparations dosage and methods of administration indications and contraindications[41] If this shows what appears to be a host of inconsistencies the complex nature of the action of digitalis should be realized However if the different circumstances that are apt to govern the clinical results are kept in mind the reasons for the variations in the action of digitalis will be better understood

Digitalis is a wonderful remedy when correctly administered a useless drug when given in too small amounts and a dangerous poison when the dose is excessive However, a broad zone of therapeutic usefulness exists between the two extremes and the amount of the drug needed to keep the patient in this zone can be gauged by careful clinical observations[6]

The action of digitalis upon the heart consists of two phases The first is a direct effect of the drug on the cardiac muscle including the bundle of His and the Purkinje fibers (modified muscle) The second consists of a stimulation of the vagus nerves for if these are cut the effect is removed

This does not mean that the second effect is necessarily a reflex action Many pharmacologists believe that digitalis stimulates the vagus center It seems certain however that it does not directly stimulate the vagus endings in the heart muscle

**The direct or peripheral effect** of digitalis appears first manifesting itself by an alteration of the T wave of the electrocardiogram This initial indication of the action of the drug may be followed by a predominance of either the vagal or the direct effect

**Vagal Effect** A study of the vagal action which in most if not all respects tends to counteract the direct effects of the drug suggests an attempt on the part of the controlling mechanisms of the heart to compensate for the action of the drug Thus the direct or peripheral action of the drug (1) increases the irritability and muscular tone (2) strengthens the contraction (3) prolongs the refractory phase of the myocardium (4) slows but strengthens conduction by prolonging the refractory phase of the conducting system The vagal stimulation (1) decreases muscular irritability, (2) weakens the auricular contractions (3) shortens the refractory phase and increases the rate but weakens the strength of conduction

In spite of this apparently opposite effect on the part of the vagus both actions coincide in interfering with conduction through the A V bundle and therefore in tending to produce A V block Consequently in auricular fibrillation the ventricular rate is slowed by the direct action of digitalis which prolongs the refractory phase of the bundle of His and by the vagal action which weakens the conduction On auricular fibrillation per se the direct effect of the drug may decrease the rate through the prolongation of the refractory phase while the vagus tends to increase the rate by shortening the refractory period The vagus effect usually predominates in the auricle increasing the rate of the fibrillation Digitalis therefore does not stop the fibrillation but actually makes the auricle fibrillate more rapidly Paradoxically this is beneficial for a speeding of the auricular rate increases the A V block and leads to further ventricular slowing

The late toxic effects of digitalis are characterized by a predominance of the direct action of the drug on the myocardium and the conducting system Consequently atropine is of no value in digitalis poisoning since the main action now is a direct muscular one

If, to the effects mentioned we add the depression of the heart's pacemaker, the sino auricular node that results from the stimulation of the vagus when sinus rhythm prevails we have all the important effects of the digitaloid drugs and the clinical observations can be explained in terms of these actions In therapeutic doses digitalis has no direct effect on the peripheral vascular tree or on the coronary arteries, however, indirectly the coronary flow is altered since the coronaries are effectually influenced by the rate and the degrees of contraction and relaxation of the heart as a whole

Clinical studies have shown that the administration of digitalis decreases the heart size both in health and in the presence of congestive failure

This effect is consistent and can be demonstrated by careful roentgen ray examinations Stewart and Cohn[3,4,3] also Harrison and his co workers[10,11] have shown that in health digitalis diminishes cardiac output and minute volume from 20 to 35 per cent while in patients with heart failure improvement is accompanied by a marked increase in the cardiac output The explanation of this apparent contradiction is to be found in the fact that under normal conditions the heart is at an optimum size for the performance of its work Digitalis decreases its size according to surface area measurements to three fourths or four fifths of the normal and to that extent lessens its output

However in the enlarged heart of decompensation, the cavities are dilated but the myocardium is weak, and the output is low Digitalis through its action on the irritability and contractility decreases the size of the cavities but not to a degree less than normal Although for the normal heart and for the heart of congestive failure with normal rhythm the increased irritability and contractility and decrease in the heart size satisfactorily explain the results obtained, for the decompensated heart the explanation must never minimize the importance of the drug s effect on decreasing A-V conduction Indeed the most profound and dependable results from digitalis occur in these cases of auricular fibrillation or flutter with decompensation when the drug decreases A V conduction to a 'toned up' ventricular muscle Clinical improvement follows the slow rate and increased power of the ventricle regardless of the auricular rate

The quantitative improvement in the circulatory rate following digitalis may be shown by simple tests based on the length of time required by certain substances injected in the median cephalic vein at the elbow to reach other areas For example if histamine is used a flush of the face may be watched for (arm to face time) if decholin is used the bitter taste of the drug may be the end point (arm to tongue time), or if ether is injected the appearance of the characteristic odor on the breath may permit a calculation of the arm to lung time to be made Calculation of the circulation time may be a valuable aid in differentiating cardiac from bronchial asthma when the diagnosis is in doubt In uncomplicated bronchial asthma the circulation time is normal (page 115)

In man, digitalis produces no important changes in the systolic blood pressure unless the previous level was either high or low and under these conditions the drug tends to bring the systolic pressure back to normal The increase in the low blood pressure would appear to be the logical sequence of the improved cardiac efficiency However the fall in the pressure level observed in some cases of the hypertensive type deserves a word of comment The failing heart in hypertension has produced a deficient circulation, which is accompanied by a poor oxygen supply to the vasomotor center An attempt on the part of this area to compensate by increased activity causes a rise in the systolic pressure Digitalis by improving the cardiac efficiency relieves the partial anoxemia of the vasomotor center, which in turn decreases its activity, and the systolic pressure

is lowered The action on the diastolic pressure is more uniform as in the majority of cases it is reduced the net result being an increase in the pulse pressure

### Toxicity

Digitalis should always be prescribed with care Unpleasant effects that are manifestations of beginning toxic action need not attend the successful therapeutic administration of the drug As Withering observed

> The sickness thus excited is extremely different from that occasioned by any other medicine it is peculiarly distressing to the patient it ceases it recurs again as violent as before—(Fig 39)

One hundred and fifty years ago Withering classified this action of digitalis as a direct one upon the stomach mucosa an opinion based upon the fact that digitalis had previously had considerable reputation as an emetic The later demonstration that large amounts of digitalis given by hypodermic injection still produced nausea and vomiting did not convince *the physicians of that day that the action was not a gastric one* for they then believed that the drug was excreted into the stomach This early *toxic action however is on the vomiting* center which becomes hypersensitive to reflexes believed by the author to arise from the heart while *others claim that they arise from the abdominal viscera chiefly the liver* All preparations of digitalis if they are active and capable of giving good *therapeutic results produce nausea and vomiting when* administered in large doses

*Anorexia* and *nausea* usually precede the *vomiting of overdigitalization* and these symptoms should serve as a warning The nausea comes in periods or waves that usually *disappear within two days* after the drug has been discontinued

In rare cases diarrhea may *appear as a toxic manifestation* of digitalis action while cerebral symptoms should be watched for particularly in older subjects *It is important to remember that these signs may* occur without the appearance first of nausea and vomiting and are due either to a direct effect on the cerebral centers or to a change in the cerebral circulation If mercurial diuretics are being administered at the same time the issue is further complicated Weiss[394] believes that the onset of the psychosis occasionally seen following the administration of digitalis accompanies circulatory improvement In his opinion the cerebral circulation is already abnormal owing to chronic sclerotic changes and the entrance into it of the toxic products mobilized during the long standing edema causes the onset of the psychosis Headaches as well as confusion may follow digitalis administration the latter progressing in some cases to delirium Loss of memory in older subjects following digitalis is not uncommon The exact cause of disturbances of vision that occasionally follow digitalis is unknown Dimness of vision distortion of colors and rarely blindness may follow large doses of the drug

( 184 )

EFFECTS, RULES, and CAUTIONS.

THE Foxglove when given in very large and quickly-repeated doses, occasions sickness, vomiting, purging, giddiness, confused vision, objects appearing green or yellow; increased secretion of urine, with frequent motions to part with it, and sometimes inability to retain it; slow pulse, even as slow as 35 in a minute, cold sweats, convulsions, syncope, death.*

When given in a less violent manner, it produces most of these effects in a lower degree; and it is curious to observe, that the sickness, with a certain dose of the medicine, does not take place for many hours after its exhibition has been discontinued; that the flow of urine will often precede, sometimes accompany, frequently follow the sickness at the distance of some days, and not unfrequently be checked by it. The sickness thus excited, is extremely different from that occasioned by any other medicine; it is peculiarly distressing to the patient; it ceases, it recurs again as violent as before; and thus it will continue to recur for three or four days, at distant and more distant intervals.

These

* I am doubtful whether it does not sometimes excite a copious flow of saliva.—See cases at pages 115, 154, and 155.

FIG 39 Page 184 of William Withering's *An Account of the Foxglove* 1785

of PATIENTS. 191

INFERENCES.

TO prevent any improper influence, which the above recitals of the efficacy of the medicine, aided by the novelty of the subject, may have upon the minds of the younger part of my readers, in raising their expectations to too high a pitch, I beg leave to deduce a few inferences, which I apprehend the facts will fairly support.

I. That the Digitalis will not universally act as a diuretic.

II. That it does do so more generally than any other medicine.

III. That it will often produce this effect after every other probable method has been fruitlessly tried.

IV. That if this fails, there is but little chance of any other medicine succeeding.

V. That in proper doses, and under the management now pointed out, it is mild in its operation, and gives less disturbance to the system, than squill, or almost any other active medicine.

VI. That when dropsy is attended by palsy, unsound viscera, great debility, or other complication of disease, neither the Digitalis, nor any other diuretic

FIG 40 Page 191 *Ibid*

192 INFERENCES.

retic can do more than obtain a truce to the urgency of the symptoms; unless by gaining time, it may afford opportunity for other medicines to combat and subdue the original disease.

VII. That the Digitalis may be used with advantage in every species of dropsy, except the encysted.

VIII. That it may be made subservient to the cure of diseases, unconnected with dropsy.

IX. That it has a power over the motion of the heart, to a degree yet unobserved in any other medicine, and that this power may be converted to salutary ends.

PRACTICAL

FIG 41 Page 19 *Ibid*

Toxic doses of digitalis cause an increase in the irritability of the myocardium resulting in the production of extrasystoles (more often ventricular than auricular) coupling or pulsus bigeminus (see Fig 248) and various other arrhythmias Large doses of digitalis may be followed by mechanisms of a much more serious nature Auricular fibrillation may appear suddenly Ventricular centers may be stimulated so that they give rise to a succession of impulses resulting in a paroxysm of tachycardia This is extremely dangerous since in some instances it may pass into ventricular fibrillation It is very easy to produce this sequence in the laboratory animal by overdosage of digitalis and it seems reasonable to suppose that the same mechanism produces death in man when care has not been used in the administration of the drug

The effect of digitalis on the sino-auricular node produced principally if not entirely through vagal action results in marked grades of sinus arrhythmia (see Fig 194) and may produce sinus arrest (see Fig 180) Large doses may markedly depress the S A node with the production of a dangerous bradycardia Rarely does the depression of the A V conduction proceed to complete heart block although I have seen this occur several times in exceptional cases following the administration of small doses of digitalis (see Fig 246)

Some investigators have reported an eosinophilia following digitalis administration[344] and claim that this is evidence of an allergic effect Possibly there are allergic reactions to digitalis, but too often the term has been used to cover our ignorance of fundamental reactions and to lull us into a complacency typical of the mind in the Dark Ages I have never seen urticarial rashes or any manifestations that would tend to suggest an allergic reaction Occasionally patients exhibit a hypersensitivity to the drug and show toxic effects following small doses (page 107) However these responses are by no means allergic Patients of this type should be managed without the use of digitalis

To the informed astute observer experience with digitalis in the clinic and at the bedside is the final teacher and as this experience increases it should be possible to employ the drug efficiently with only an occasional need for a cardiologist or the electrocardiograph

### Pharmaceutical Preparations

It is an unnecessary waste of time for the busy practitioner to attempt to familiarize himself with all the different digitalis preparations that flood the market Every one that is fit to use at all has essentially the same action Furthermore many of the proprietary and imported brands are too expensive for the patient in moderate circumstances Since digitalis in many cases once begun will be continued for a long time it is wise to start with a dependable inexpensive preparation This is the U S P whole powdered leaf in capsule or made up in pills or tablets The U S P tincture is equally efficient but it is not as convenient has an unpleasant taste does not keep as well and the dosage is not as easy to regulate The claims

of the representatives of different drug houses that their preparations of digitalis *do not produce nausea and lack the bad effects of the numerous* other preparations of the drug that patients are in danger of having handed to them across the drug counter as far as I am concerned fall on deaf ears Solubility tests, that salesmen come prepared to perform before my eyes with the premise that the test tube in the hand represents the stomach leave me unmoved On occasion I have been informed that I fail to understand and appreciate the great amount of trouble and research that their company has been through to bring this special preparation of digitalis to me in its purified state In any event my primary interest is still in the pills made from the USP whole powdered leaf of digitalis which assures their potency and the only test I put them to is to make certain that they can be readily crushed between the fingers If so they are satisfactory It is well to keep in mind that the patient can be saved money when the maintenance dosage has been established by prescribing digitalis in quantities sufficient to last several months Always prescribe digitalis alone and not in a preparation containing other ingredients for variation of the daily dosage is difficult in the presence of other drugs Finally attention should be called to the fact that the per Gm potency of the USP XI digitalis exceeds that of the USP X preparations by 25 to 30 *per cent*[88] *One hundred milligrams of USP XI digitalis powder contain* one USP unit of digitalis which is identical with the international unit

### Dosage

*The dose of digitalis is governed by the degree of cardiac failure and* the susceptibility of the patient Eggleston advised one cat unit of digitalis (approximately 80 mg of USP XI powder or 0 8 cc of USP XI tincture) for each ten pounds of body weight less the estimated amount of edema fluid present but this amount should be regarded as approximate only It is safe to say that the amount of digitalis whole leaf necessary for the complete digitalis effect in an adult of average weight lies between 0 75 to 1 50 Gms (12 to 24 grains) At the first visit I generally prescribe 24 of the 0 1 Gm (1½ grains) tablets of digitalis whole leaf During the first 24 hours ten of these may be given during the next 24 hours 0 5 Gm (7½ grains) may be taken The patient then should be carefully watched since the amount that has been given is close to or equivalent to that needed for the therapeutic digitalization If the occasion is not an emergency one tablet 0 1 Gm (1½ grains) may be prescribed after each meal for one week and the patient examined carefully at the end of this time It is not wise to calculate the desired amount of digitalis by the Eggleston method send the patient away and trust that he will experience no untoward effects until seen again Good treatment today does not consist in pushing the digitalis until it acts on the kidneys stomach pulse or bowels and in this respect we are forced to depart slightly from the rules laid down by Withering

Observation usually tells us when we are reaching the maximal thera

peutic dose The pulse slows (particularly where fibrillation is present) to 70 beats per minute or less Diuresis appears as the congestive phenomena fade There may be anorexia The amount should then be cut to 0 1 Gm (1½ grains) daily This is the so called maintenance dose and it can in most cases be continued indefinitely Of course, exceptions occur and the exact amount of the maintenance dose will have to be adjusted to the patient by experiment for it will depend on the amount of the drug excreted and destroyed in the body daily For the average patient this figure will be found to vary between 0 06 and 0 18 Gm (1 to 3 grains) Variations occur in each case and the amount may even be different in the same patient under varied circumstances Adjusting this maintenance dose of digitalis is one of the physician s important duties at each follow up examination

Where auricular fibrillation has been present and the rate reduced to 70 by digitalis the patient will be much relieved At this stage of treatment the physician should take the necessary time to explain the aims of therapy and the action of digitalis for it is possible to train the patient to become skilled in the matter of maintenance dosage It is not dangerous to make a student of the pulse out of the patient with chronic auricular fibrillation since much of his future efficiency depends on the successful use of digitalis just as the future of the diabetic depends on the accurate balance between insulin and diet Education of the patient in all matters concerning his disease is invaluable in both instances

The physician should govern the dose of digitalis he prescribes by the interval between visits Large doses should not be given unless it is certain that the physician will go to see the patient the next day Ambulatory patients in clinic or private practice as a general rule should be slowly digitalized

When it is necessary to digitalize a child the amount per pound of body weight in some cases may be found to be greater than that needed for the adult owing to the higher metabolic rate of children This amount has been variously estimated but again EACH CASE SHOULD RECEIVE A DOSAGE DEPENDING ON THE CLINICAL SYMPTOMS AND THE OBSERVED EFFECT OF THE ADMINISTRATION In my experience digitalis does not have the dramatic results in children that are observed in adults This may be due to the rare occurrence in children of auricular fibrillation and flutter

It is just as serious an error to give amounts of digitalis too small to be of value as it is to produce toxic effects While the modern tendency seems to be to prescribe large doses occasional cases are seen in consultation where the doses administered could have no influence whatsoever on the course of the cardiac failure In these instances good results invariably follow increase in the digitalis The administration of too small doses generally occurs in cases where the tincture has been prescribed and the amount to be taken stated in drops Drops will be found to vary according to the type of dropper the temperature the rate of dropping and the

angle of the dropper If the tincture must be used, always have the patient measure the dose in a graduated dropper or medicine glass

INDICATIONS

When digitalis is needed the method of saturation or digitalization that has been described is the only satisfactory way to prescribe the drug When the patient is not showing signs of failure small daily 'tonic' doses have been recommended [7] It may be quite possible to secure tonic effects in patients with organic heart disease of the hypertensive or rheumatic type and in this manner to delay the appearance of dilatation These opinions however are based mainly on animal experimentation and there exists as yet no satisfactory proof that small daily doses in man have the same beneficial action Except in the presence of auricular fibrillation or flutter I have not given digitalis to a patient with organic heart disease in the absence of signs of failure

Rarely is it necessary to employ any other preparation of digitalis than the powdered whole leaf by mouth Sometimes gastro-intestinal disturbances attending congestive failure call for the temporary adoption of another method of administration and in these instances the digitalis may be given by rectum Levy [1] finds digitan an aqueous solution of digitalis to be less irritating to the rectal mucosa than the alcoholic solution of digitalis The equivalent of about 0 1 Gm of the powdered leaf is contained in 1 cc of digitan Consequently following a cleansing enema an amount can be given up to 20 cc through a rectal tube If the digitalis is given in the tincture form it must be well diluted to prevent irritation (approximately one volume of tincture to four volumes of physiologic saline) Absorption by rectum is usually good and the speed of action is comparable with that observed when similar doses are given by mouth

Intramuscular injections of digitalis preparations are painful I quite agree with Fishberg[100] that this route is indicated only when it is impossible to enter a vein

If there is a contraindication to the rectal administration and the emergency is great the intravenous route may be used provided the patient has not been receiving digitalis during the previous week

**Strophanthin** (U S P ) is the preparation of choice for intravenous injection The initial dose should not exceed 0 5 mg (1/120 grain) and 24 hours later 0 3 mg may be given to maintain the effects of the drug When strophanthin is given intravenously effects may be observed within ten minutes It is a good plan when using this method to dissolve the strophanthin in 10 to 20 cc of a 10 per cent dextrose solution and inject slowly As soon as digitalis can be taken by mouth the daily injections of strophanthin are discontinued Brams and his associates[40] have shown however that daily injections of 0 3 mg for as long as 24 consecutive days failed to produce significant clinical or electrocardiographic evidence of toxicity

The pharmacologic properties of strophanthin are identical with those

of digitalis Since strophanthin administered intravenously has a much faster action than digitalis given orally, it has a definite place in emergencies (page 398) In paroxysmal dyspnea and sudden congestive failure excellent effects may be obtained I have seen two dramatic results follow the use of intravenous injections of strophanthin in the receiving ward Both patients were women who developed sudden cardiac failure in the last months of pregnancy and who had not been receiving digitalis previous to admission I have also seen poor results follow the use of strophanthin in some patients who had postoperative tachycardia and in others who had organic heart disease but no evidence of congestive failure

Ouabain a crystalline glucoside from g strophanthin is injected in one half the dose recommended for strophanthin The strophanthins are less irritating and less cumulative than digitalis but their absorption is so uncertain that their use by mouth is not advised

Squill prepared from the bulb of the sea onion (*Scilla maritima*) has enjoyed a reputation as an efficient therapeutic remedy in a variety of conditions Although employed for centuries in the treatment of dropsy its real value in the management of heart disease and its position as a member of the digitaloid group were factors not fully recognized until 1865 The water insoluble glucosides of squill (scillaren A and B) were isolated in 1934

Recently Chamberlain and Levy [4] have called attention to the use of URGININ which is a mixture of equal proportions of the two active water insoluble glucosides crystalline scillaren A and amorphous scillaren B This preparation can be obtained in tablets containing 0 5 mg (1/120 grain) of the mixed glucosides Assay by the cat method has shown that one of these tablets has an average potency of 2 13 cat units

The results obtained by the use of urginin in cases of congestive failure are similar to those obtained following the administration of digitalis Diuresis is produced and the ventricular rate is slowed particularly in the presence of auricular fibrillation Levy and Chamberlain found that the average total effective dose of urginin is 9 0 mg (18 cat units) and the daily maintenance dose is between 0 5 and 2 0 mg in the presence of auricular fibrillation and 1 5 mg in cases with sinus rhythm Large single doses of urginin are apt to cause gastric disturbances It is best to give 1 5 mg (three tablets) three times daily after meals for two days 1 0 mg (two tablets) twice daily until the desired clinical effects are obtained *and then continue with 0 5 mg (one tablet) twice daily* as maintenance dose As in the case of digitalis therapy the plan should be changed to fit the individual patient Urginin offers no advantages over digitalis in cases of congestive failure and rectal administration of this preparation is unsuccessful

Urginin has toxic effects similar to digitalis Vander Veer and his associates [378] reported the occurrence of nausea vomiting and diarrhea in patients on maintenance doses of urginin They also observed characteristic toxic arrhythmias ventricular tachycardia coupling of ventricular prema

ture beats and auricular fibrillation These manifestations depend largely on the severity of the cardiac damage and the care with which the drug is given Patients who have slightly damaged hearts may complain of nausea and vomiting before any disturbances in cardiac rhythm are noted On the other hand when severe myocardial damage is present, dangerous arrhythmias may appear before the calculated amount of the drug has been given Although idiosyncrasy is fortunately rare we do meet patients at times who exhibit a prejudice against the use of digitalis In these instances urginin may be prescribed

It is well to remember that all digitalis preparations deteriorate with age Powdered leaf of digitalis if kept dry seems to be less affected than other preparations which is another consideration that recommends it for routine use Levy [1] calls attention to the rapid deterioration of aqueous solutions of k strophanthin and of certain digitalis preparations when stored in ampules of soft glass presumably caused by the alkali absorbed from the glass Ampules of hard glass should always be used for these drugs

### CONTRAINDICATIONS

Heart failure is not very often accompanied by situations that contra indicate digitalis therapy There are other conditions however where the use of digitalis in the absence of signs of heart failure may be harmful In cases of partial heart block if there are present seizures that suggest Adams Stokes attacks the drug should not be used It is no longer con sidered good practice to give digitalis in pneumonia unless the condition of the heart specifically requires it [4 4] Digitalis may be harmful if given to patients who have angina or coronary occlusion in the absence of conges tive manifestations Caution should be used in giving large doses of calcium[38 133 3 1] or ephedrine[1 4] to patients who are being digitalized Deaths have been reported in cases where intravenous calcium has been given to digitalized patients In diphtheria digitalis should be given with great care since diphtheria toxin and digitalis have somewhat similar effects on the heart

Some surgeons continue to increase the hazards of their anesthesias by giving digitalis routinely by mouth before operation and intramuscularly upon the slightest provocation postoperatively It is without value in the absence of congestive failure pre-operatively and most of the tachycardias I have seen postoperatively arise from shock and other extra cardiac causes where digitalis cannot be expected to be effective and in many instances is actually harmful Except in the presence of a specific cardiac indication digitalis is contraindicated with ether or chloroform These anesthetics increase vagal tone When the augmented vagal activity result ing from digitalis is imposed upon the exaggerated vagal activity of the anesthetic a slight stimulation of the vagi may produce a prolonged diastolic pause If this is preceded by a deep inspiration a fatal exposure of the myocardium to the influence of the anesthetic may be the result

## DIURETIC DRUGS

When the combined measures of bed rest and digitalis do not suffice in removing all edema fluid and restoring cardiac balance, we have at our command a group of drugs whose diuretic properties lend valuable assistance The new members of this group of diuretics have already displayed so high a degree of efficiency combined with so low a toxicity that they are rapidly replacing the older drugs as well as some of the older methods of therapy For this reason Southey s tubes are rarely needed by the modern practitioner and scarification for the relief of extensive edema is seldom required

The diuretic drugs may be conveniently grouped as the xanthines the inorganic salts urea and the organic mercurials

### Xanthines

Members of the xanthine group have a low toxicity and may be administered by mouth but often their action is disappointing The least toxic most efficient and the least expensive member of the group is theobromine sodium acetate It is administered as a tablet or a powder or in a capsule in doses of 0 5 Gm (7½ grains) three times daily

Theophylline with ethylenediamine (aminophylline) is likewise a potent member of this series that can be given orally in doses of 0 1 Gm (1½ grains) three or four times daily or intravenously in doses of 0 24 Gm in 10 cc of physiological saline

Theophylline (theocin) is used in oral doses of 0 2 Gm (3 grains) three or four times daily although it is likely to prove nauseous to some patients

Theobromine calcium salicylate (theocalcin) causes less gastric disturbance and may be given in 1 0 Gm (15 grains) doses after meals

The mechanism of diuretic action of the xanthines may involve several factors the relative importance of which may change under different conditions These factors for which we have at present adequate experimental evidence may be briefly summarized as follows (1) An increased glomerular filtration due to the elevation of the intraglomerular pressure (2) An increase in the number of the functioning glomeruli (3) A decreased tubular absorption (4) An increase in the non-colloidal constituents of the blood

It is best to give a xanthine preparation as long as its effect is maintained in the absence of untoward effects Many clinicians administer members of this group in full doses for three to five days They are then withdrawn and used subsequently as indicated over a similar period

### Inorganic Salts

**Chlorides and Nitrates** Important among the saline diuretics are the chlorides of ammonia potassium and calcium and the nitrates of ammonia and potassium each of which should be given orally The presence of these salts in the blood raises the osmotic pressure of the

plasma with the result that water from the tissues and lymph is transferred more rapidly to the blood transported to the kidneys where it passes with the salts into the glomerular filtrate The tubules refuse to absorb the unneeded salts hence they with the water they withdraw from the tissues pass from the body

When the ammonium salts or calcium chloride are used the typical salt effect is augmented by an acidosis the extent of which will depend upon the amount of the salt administered Theoretical objections can be raised against the use of nitrates which in rare instances may in part be changed to nitrites by the intestinal flora and also to the potassium salts which although entirely nontoxic when administered orally to the normal patient might accumulate in some cardiac cases with decreased renal function in sufficient quantities to embarrass the heart While I consider these effects highly improbable ammonium chloride is the saline diuretic of my choice When administered alone in large quantities ammonium chloride is apt to cause gastric irritability consequently it is better to give it in the form of an enteric coated tablet of 0 5 Gm (7½ grains) Two or three of these administered after meals and at bedtime usually cause no disturbance of digestive function In some patients a daily dose of 10 Gms may be required to produce a satisfactory diuresis

## Organic Mercurial Diuretics

Paracelsus used mercury in the treatment of edema as early as the sixteenth century The success he achieved may be judged when we consider the extensive use of mercury for all diseases in the centuries that followed William Stokes in 1854[3 8] again called attention to the valuable diuretic properties of mercury when he stated

> It happens again and again that the exhibition of mercury as by enchantment removes the anasarca

Mercury is an ingredient of the famous Guy s pills but its real value as a diuretic was not appreciated until the recent discovery of the less toxic organic preparations In 1920 Saxl and Heilig[2 8] introduced the first of these compounds known as novasurol (merbaphen U S P) and verified the earlier statement of Stokes that mercury "as by enchantment removes anasarca About 1927 salyrgan (mersalyl) was introduced on the justification that it was less toxic in laboratory and clinical experiments but the inclusion of merbaphen in the latest edition of the U S P is sufficient evidence of the usefulness and safety of the older drugs During the next year (1928) a preparation containing an organic mercurial salt combined with theophyllin was introduced by von Issekutz and von Vegh[1 1] known as mercupurin All these preparations are ineffective when given by mouth and must be administered intravenously or intramuscularly Recently (1934) Engel introduced a suppository containing mercupurin without the theophyllin this is known as *mercurin*[53 98]

Mode of Action The mercurial diuretics owe their therapeutic value to the fact that they ionize feebly under appropriate conditions to form

mercury ions Although these ions have a general affinity for all proteins their action is manifest principally on the kidney tubules suggesting that here the body presents optimal conditions for the ionization and action of these drugs with the result that reabsorption of the glomerular filtrate is diminished producing a tubular diarrhea

Experiments have demonstrated that the primary site of action of these drugs is not extrarenal If we transplant a kidney of a novasurol treated dog into the neck of a normal dog we will find that the novasurol kidney excretes much more urine than the dog s other kidneys conversely if a normal kidney is transplanted into a novasurol injected dog it will excrete much less than the dog s kidneys which had been exposed to novasurol

Technic of Administration While three methods of administration have been proposed (intramuscularly intravenously and by rectal suppository) I have obtained the best results from the intravenous route If care is used at all times in making the injections local reactions as well as the sclerosing effects these preparations have on the veins can be prevented LEAKAGE INTO THE SUBCUTANEOUS TISSUES DURING INTRAVENOUS INJECTION SHOULD BE ALWAYS BE AVOIDED SINCE THESE AREAS ARE SUBSEQUENTLY MOST PAINFUL AND NOT INFREQUENTLY SLOUGH

The equipment necessary for an intravenous injection of any of these mercurial diuretics is simple and may be sterilized and carried to the bed side of the patient in a small container Sterilization of the skin with alcohol is sufficient With the tourniquet in place the needle is held parallel to the veins and inserted When the needle is completely in the vein as shown by the column of blood entering the syringe the tourniquet is released and the injection slowly given In case the veins are deeper owing to the thick subcutaneous tissues a longer needle (1 inch 24 gauge) should be used In patients who have excessive edema or obesity and when other points of entry are obscured the injection may be given successfully into a vein on the back of the hand.

The initial intravenous dose of mercupurin or salyrgan should be ½ cc to 1 cc of the 10 per cent solution Untoward reactions are rare and subsequent doses of 2 cc can be administered safely at intervals of three to six days It is usually unnecessary to give the drugs at intervals of less than three days In cases where intravenous injection is impossible the intramuscular route may be used The dosage is the same Intra muscular injections of mercupurin are best given into the upper outer quadrant of the buttock (see Fig 92) using a 2 to 2½ inch needle of 22 gauge Although this method is more painful a similar diuresis is produced

When there is an objection on the part of the patient to parenteral therapy suppositories may be tried although I have not observed as satis factory results following their use as reported by others [110] However in cases where a good diuretic response follows suppositories have a distinct advantage since it is then possible to give up the intravenous route—always a desirable step when another avenue of administration proves as effective The use of suppositories means fewer visits of the patient to

the clinic or physician's office and consequently results in a saving of time and money The suppositories are made of a cocoa butter base, and contain 500 mg of the mercurial salt of mercupurin without the addition of theophyllin The suppository should always be inserted in the morning after a cleansing enema in which event absorption may be fairly rapid Diuresis starts in one to two hours The use of suppositories should be guided by the physician depending on the amount of edema present and its tendency to recur Intervals of four to six days are usually recommended

The acid producing salts are weaker diuretics in themselves but have been found to augment considerably the diuresis if administered with the organic mercurial diuretics Keith Barrier, and Whelan[18] first used ammonium chloride in combination with novasurol and obtained good results when either preparation given alone was ineffective The mechanism of this synergistic action is probably related to the pH of the glomerular filtrate Other acid forming salts like ammonium nitrate and calcium chloride were found to be just as effective as ammonium chloride Administration of alkalis has been shown to reduce the diuresis Whenever possible the acidifying salt ammonium chloride is given in 1 0 Gm (15 grains) doses after meals and at bedtime for two days before the administration of the mercurial diuretic

UNTOWARD EFFECTS The addition of these powerful agents in the form of mercurial diuretics to our therapeutic program has been a great advance However caution should be used in their indiscriminate use, particularly in older people Too rapid dehydration in some instances has been followed by extreme weakness and not uncommonly by changes in the mental condition of the e patients They lose interest take little food and may at times show a tendency to an increasing stupor leading eventually to coma The enormous loss of sodium chloride and water from the body must be considered as one of the dangers of this form of therapy[30] In addition to the weakness and thirst complained of by the patient, dry tongue sunken features and other signs of dehydration should be looked for At times the chloride loss with its accompanying weakness simulates Addison's disease where a chloride deficiency likewise occurs

The sodium ion is linked with the fundamental biochemical processes of life and one of its chief roles is to hold water in the intercellular tissue spaces The administration of one of the diuretic drugs causes the loss of sodium chloride from the tissues the amount depending on the dose of the drug Consequently when the symptoms described above appear in any patient receiving mercurial diuretics the usual routine therapy should be interrupted, and water and sodium chloride administered by mouth or intravenously as the occasion demands

In the treatment of congestive failure it is well to remember that all the procedures recommended should not be carried out during too short a period of time for example thoracentesis abdominal tap diuresis and phlebotomy This is particularly true in aged patients I have seen weakness and collapse follow 'too much doctoring a state of affairs similar to

that produced by the repeated bleedings of our fathers of old ' It is wise to make haste slowly and not try all the drugs in the saddle bag during the first 24 hours

It is not my purpose to arouse any apprehension on the part of the physician in regard to the mercurial diuretics No great concern should attend their daily use in practice when definitely indicated if the above precautionary measures are followed In very sick patients particularly those who suffer from attacks of paroxysmal cardiac dyspnea (cardiac asthma) all intravenous injections should be made slowly It might be well in some cases to dilute the drug to 10 cc with normal saline solution However if not less than three minutes are allowed for the injection most of the organic mercurial diuretics may be used undiluted in the average patient Injections of mercurials may be given at the usual intervals over the course of many years with no untoward effects as accumulating reports in the literature point out (page 113) Rare cases have shown a renal mercurial poisoning[417] but I have never seen this occur Post mortem examinations of the kidneys of patients who have been receiving many injections show no toxic change[3]

Indications for Mercurial Diuretics Cardiac edema is the chief indication for the use of these drugs At times when the administration of digitalis is not tolerated (page 107) the organic mercurials hold a place of prime importance in the schedule of therapy

In certain types of dyspnea particularly the nocturnal variety much can be gained from the use of the mercurial diuretics These attacks of nocturnal dyspnea which frequently complicate left ventricular failure may be prevented by the routine administration of the mercurial diuretics I have seen this beneficial result occur even when edema was not in evidence (page 109)

I believe that the mercurial diuretic group has likewise helped to provide a lengthn d day for the cardiac patient who was previously incapacitated at an earlier date by persisting edema If edema remains after the full exhibition of digitalis in patients with regular rhythm the mercurials form the sheet anchor in therapy in any type of heart disease Mercurial diuretics likewise have a place in the edema of nephrosis where the kidneys can excrete urine of a specific gravity of 1 016 or over and where evidence of acute nephritis is absent

Ascites resulting from both cardiac and noncardiac causes calls for the trial of the mercurial group In these cases the result will usually not be as dramatic as is seen when edema fluid is removed from other locations particularly where the ascites is secondary to hepatic disease After an initial abdominal tapping the routine use of a mercurial diuretic may make the repetition of this procedure unnecessary or it may markedly increase the interval between tappings (Case 7)

Contraindications Hematuria seems to be the sole contraindication to the use of mercurial diuretics according to some authorities[1 3] However caution should always be used in older patients especially in the presence

of cachexia fever enteritis or colitis, and hemiplegia Where local rectal conditions (inflamed or thrombosed hemorrhoids, rectal fissures) are present *the use of the suppositories is contraindicated Care should be* taken to prevent spontaneous redigitalization following administration of mercurial diuretics (page 113)

PREPARATIONS MERBAPHEN U S P or novasurol is a compound of mercury with barbital It contains about 34 per cent mercury and is marketed in ampules containing 1 and 2 cc of a 10 per cent solution

SALYRGAN or mersalyl is a fine crystalline powder containing not less than 37 6 per cent of mercury in poorly ionizable form Ampules containing 1 or 2 cc of a 10 per cent solution are obtainable Salyrgan has been recently modified and now is reported to consist of a 'complex compound of mercury and sodium salicyl allyl amino-o acetate in a five per cent theophyllin solution

MERCUPURIN is marketed in ampules each containing a 10 per cent aqueous solution of the preparation One cc contains the equivalent of about *39 mg of mercury in poorly ionizable form The theophyllin in* mercupurin is chemically bound to the mercury atom Mercupurin is supplied in 1 1 cc and 2 2 cc ampules

MERCURIN SUPPOSITORIES Each suppository contains 0 5 Gm mercurin equivalent to about 0 2 Gm of mercury or approximately two and one half times the amount of mercury contained in 2 2 cc of the parenterally administered mercurial diuretics It is supplied in boxes containing five and 25 suppositories

ESIDRONE[380 381] is a stable, neutral crystalline substance which is easily soluble in water *It contains 31 2* per cent mercury in nonionizable form and 28 0 per cent theophyllin which is chemically connected with the mercury atom Generally 1 cc of Esidrone administered intravenously or intramuscularly (never subcutaneously) produces gratifying results although 1 5 cc or 2 0 cc may be administered with comparative safety Esidrone may be given one two or even three times per week It is marketed in ampules of 1 cc (1 cc equals 0 14 Gm Esidrone equals 0 043 Gm mercury) Each ampule contains sufficient amount to allow withdrawal and administration of 1 cc

## MECHANICAL THERAPEUTIC MEASURES

**Venesection** A better understanding of the use of digitalis and the discovery of the effectiveness of organic mercurial diuretics have forced one of the oldest of therapeutic procedures almost into the discard Although previously advised in every disorder to which the human flesh is heir blood letting is now practiced only in the presence of venous hypertension that follows right ventricular failure In these acute episodes the relief obtained following the withdrawal of 500 to 600 cc of blood is at times dramatic

The procedure of venesection itself usually offers no difficulty A needle of large caliber is preferable and care should be used in applying the

tourniquet in order that the blood flow in the artery is not shut off An *inflated blood pressure cuff* makes a convenient tourniquet for ordinary purposes In emergencies a longitudinal incision into the vein serves just as well as venous puncture The amount of blood to withdraw depends on the clinical condition of the patient and is often not as important as the speed with which it is removed Usually observations of the neck veins furnish a rough gauge of the height of the venous pressure but before venesection is repeated a more exact estimation should be made whenever possible (page 54) Bloodless venesection produced by placing tourniquets

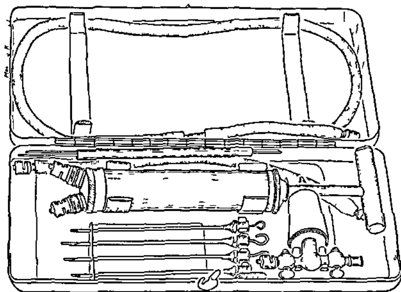
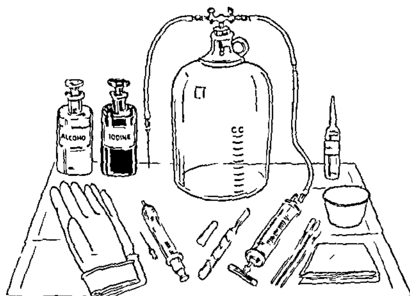


FIG 42 Thoracentesis outfit (Potain)

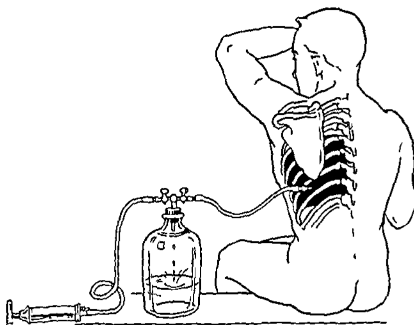
on the arms and legs close to the trunk does not give the same fall in venous pressure in cardiac failure

**Thoracentesis** Digitalis and diuretics although often efficient in preventing the accumulation of fluid in the pleural cavities usually fail to remove large collections present when the patient is first seen These require drainage inasmuch as they reduce the vital capacity and increase the amount of dyspnea Properly carried out thoracentesis should cause the patient very little discomfort

I prefer the Potain apparatus (Fig 42) that enables the removal of the fluid by a closed (siphonage) system A tightly fitting rubber stopcock is essential for success of this method One outlet is attached to the aspirating needle the other to a small suction pump A vacuum is first created in the bottle by closing the stopcock leading to the needle and pumping out the air With the patient sitting up in bed (Fig 43) the site for puncture is




A



B

Fig 43 Thoracentesis
A Essential equipment
B Technic of procedure

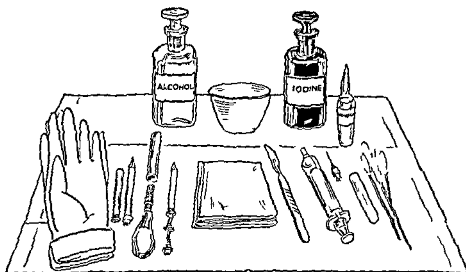
carefully selected (usually the eighth or ninth interspace in the posterior axillary line) and sterilized with iodine and alcohol Satisfactory local anesthesia is produced by infiltration of the skin and deeper structures with a 1 per cent procaine hydrochloride solution A small 26 gauge needle should be used for the skin and subcutaneous tissues and then changed to a one and one half inch length of the same gauge when anesthetizing the deeper structures down to the pleura The needle used for the tap should not have too long or too sharp a point in order to avoid puncturing the lung and producing a pneumothorax This danger, with ordinary care is remote A small incision previously made in the anesthetized skin with a scalpel allows an easier and more deliberate entry of the needle into the chest Before inserting the needle the suction in the bottle should be tested by using sterile water taking care to turn the stopcock on the side of the needle to the open position and to close the stopcock leading to the hand pump

The amount that can be safely withdrawn from the pleural cavity varies in each instance As much should be taken as possible without producing untoward symptoms During a thoracentesis the patient should be carefully watched for increase in dyspnea cough faintness or tachycardia Nausea vomiting pulmonary edema and the so-called pleural shock are possibilities but are rare (or else I have been fortunate) When the lung can be felt coming down and striking the end of the needle or if the patient begins to cough it is well to stop the procedure Withdraw the needle and seal the puncture with collodion A fall in the venous pressure may indicate improvement even after the withdrawal of as little as 400 cc It is well not to withdraw amounts in excess of 1000 cc at one time

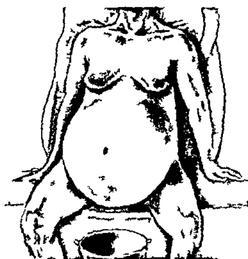
**Abdominal Paracentesis** Small collections in the peritoneal cavity usually show better response to diuretics than thoracic collections owing to the fact that the peritoneum is a better absorbing surface than the pleura An advanced degree of ascites may be present in chronic congestive failure but chronic constrictive pericarditis usually produces the largest collections If the ascites interferes with breathing it should be removed after the pleural collections have been successfully drained

The technic of abdominal paracentesis is simple and there is no contra indication to performing the operation in the home Before proceeding it is essential to have the patient empty the bladder Figure 44A shows the minimum equipment required The operation is carried out best with the patient sitting on a chair or on the edge of the bed A firm satisfactory back rest should be obtained (Fig 44B) The legs are separated and a large rubber sheet or piece of oil cloth fitted around them A household bucket is placed between the feet The skin area below the umbilicus is sterilized in the usual manner with iodine and alcohol (taking care to protect the genitalia) and the site of puncture midway between the umbilicus and the symphysis selected This area is infiltrated with one per cent procaine hydrochloride solution using a 26 gauge needle and followed by injection of the deeper areas using a 24 gauge 1½ inch needle A small incision

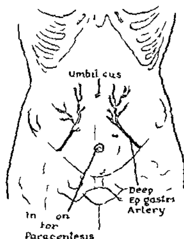
through the superficial tissues is made with a scalpel This point in the technic is important and if carried out will give the patient less discomfort




A



B



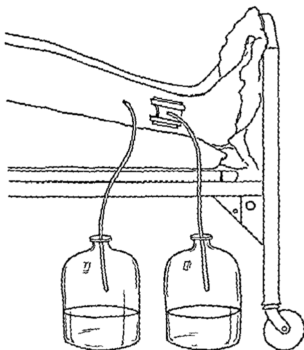

C

Fig 44 Abdominal paracentesis
A Essential equipment
B Position of patient
C Anatomic landmarks

when the trocar is inserted The incision should be large enough to accommodate the trocar which is gradually forced into the abdominal cavity by a series of controlled rotary movements When the cannula is removed



A



B

Fig. 45. Southey's Tubes
A. Essential equipment
B. Tubes in place in subcutaneous tissues

from the inside of the trocar the column of fluid escapes from the end as a jet and can be directed toward the bucket Abdominal paracentesis usually causes no discomfort The withdrawal may be momentarily checked by reinserting the cannula into the trocar taking care to follow aseptic technic continually If the flow of ascitic fluid stops suddenly this same procedure should be employed to displace small pieces of omentum that block the end of the trocar After all the fluid has been withdrawn a sterile dressing is placed over the wound and an abdominal binder applied Following abdominal paracentesis it is a good practice to keep the patient in bed until the next day

**Southey s Tubes** Cases will rarely be met where digitalis and diuretics fail to make an impression on a chronic edema of large proportions In such instances Southey s tubes may be inserted These are small hollow cannulas 5 cm in length and 3 mm in width with a series of openings in the walls (Fig 45) A point on the outer aspect of each leg about two inches above the ankle is anesthetized with procaine hydrochloride and the cannulas are inserted on a small trocar that is withdrawn as soon as the cannulas are in place Sterile rubber tubes leading to bottles attached to the side of the bed are now tied on the end of the cannulas using a fine silk thread The sides of the tubes are kept clean and are surrounded by sterile gauze Occasionally large amounts of fluid (four or five liters in 24 hours) may be drained from the tissues in cases of severe congestive failure by the use of this method

## OXYGEN THERAPY

In the uncomplicated case of chronic cardiac failure oxygen deficiency as determined by an estimation of the degree of saturation of the arterial blood is not present consequently the administration of oxygen is of no value Where there are pulmonary complications (emphysema edema infection infarction) or in cases of coronary occlusion a diminished oxygen saturation may exist in which event the inhalation of high con centrations may be most beneficial It has been shown by Barach and his associates[1, 13, 16] that oxygen in some cases of cardiac failure relieves the dyspnea and cyanosis slows the pulse promotes diuresis and diminishes edema This effect may be noted three hours after inhaling an atmosphere containing 45 per cent of oxygen Some of these patients when returned to an atmosphere containing a normal amount of oxygen have been reported to show a decreased urinary output and a return of the edema If again placed in the tent a second diuresis often follows As a rule cases of heart failure where an acute rheumatic process exists do not show the same speedy response to oxygen therapy as the arteriosclerotic type

The use of oxygen therapy combined with thyroidectomy for various types of heart disease[17] has been suggested by Barach and his associates Intensive treatment in an oxygen tent preceding and following operation

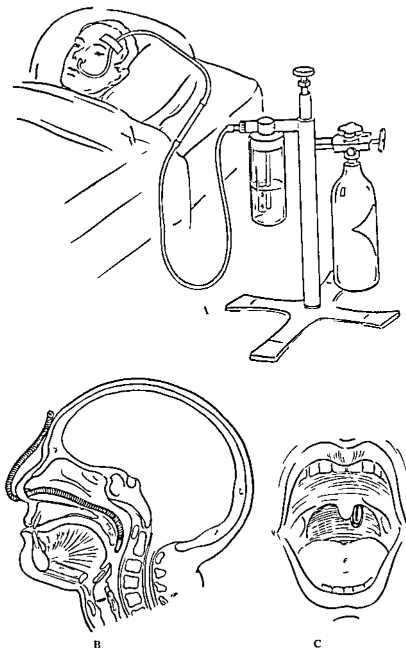



Fig 46 The administration of oxygen by the nasal catheter method
A Bedside apparatus Catheter in place
B Side view showing position of catheter
C Position of catheter in nasopharynx

makes full use of the effect of an atmosphere rich in oxygen on circulatory function

Cyanosis and dyspnea are the most reliable guides to the use of oxygen therapy in the presence of congestive failure with pulmonary complications Cyanosis and cardiac pain serve in the same capacity in cases of coronary occlusion

In congestive failure it is my impression that variable results follow the use of oxygen In some cases the cyanosis may clear up but the dyspnea may remain unrelieved while in other cases both symptoms may show a gradual improvement

Levy and Barach[13] have shown that oxygen in acute coronary occlusion is of decided benefit Here inhalation of a 50 per cent mixture supports the heart damaged by anoxemia and consequently relieves the pain A 50 per cent oxygen mixture is recommended in the average case although a 70 per cent mixture can be used if marked anoxemia is present The high concentrations of oxygen (80 to 100 per cent) are apt to cause pulmonary irritation if long continued, while the concentrations below 50 per cent do not have the same beneficial effect

**Methods of Administration** The simplest method to administer oxygen efficiently is by *means of the nasal catheter* The entire equipment consists of a cylinder of oxygen, a suitable regulating valve a humidifier and catheter with connecting tubing (Fig 46A) The supervision requires no special training and the oxygen concentration delivered to the patient compares favorably with the more expensive equipments Care must be taken to place the catheter correctly in the oropharynx Rovenstine[3] suggests that the distance between the external nares and the tragus of the ear (4½ to 5½ inches) be measured on the patient and marked on the catheter before it is inserted A good supply of olive oil or *cottonseed oil is applied to the catheter and with the oxygen flowing* this is introduced slowly through the nares to the mark previously mentioned (Fig 46B) If pushed beyond this point the stimulation produced will usually cause the patient to make swallowing movements The catheter is then withdrawn slightly to the point where deglutition does not occur and fastened in place (Fig 46C) A fresh catheter should be inserted at least every 12 hours and the nostrils used alternately A flow of oxygen of five to six liters per minute gives an alveolar concentration of 50 to 60 per cent With the flow cut down to four liters per minute a 30 to 40 per cent alveolar air concentration is obtained *Barach* believes[9] that the nasal catheter method of administering oxygen in the absence of a tent is the most efficient and recommends a flow of five liters per minute

Various types of small masks for oxygen are on the market[50 68] The mask designed by Boothby Lovelace, and Bulbulian[6 43 2 8] is efficient and satisfactory and where co-operation can be obtained from the patient most economical (Fig 47C) Enough moisture remains in the mask from the wearer's exhaled air to provide for a sufficiently high and comfortable

humidity The disadvantage of the use of the mask is the interruption necessary for frequent feedings

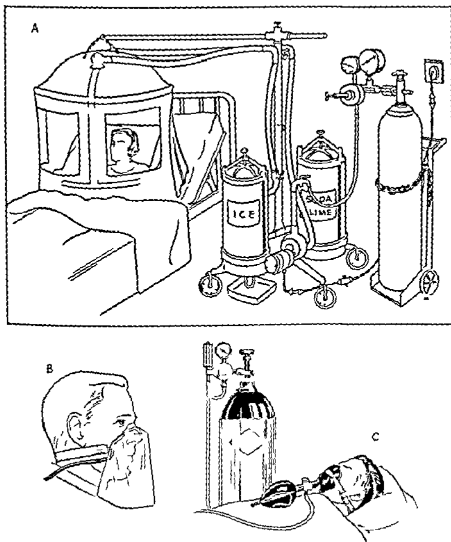



Fig 47 The administration of oxygen
A Oxygen tent
B Small oxygen face tent
C Face mask (Courtesy Ohio Chemical & Manufacturing Company)

A small oxygen face tent has been designed by Barach[10] which is inexpensive and more comfortable than the nasal catheter It is easy to remove and reapply with immediate building up to the oxygen concen

tration desired The material is transparent and light and may be comfortably molded to the face (Fig 47B)

The administration of oxygen concentrations between 50 and 70 per cent over long periods can be carried out most comfortably and efficiently by the use of the oxygen tent (Fig 47A) The observations of temperature and the humidity that are necessary require the services of a special nurse or attendant consequently this equipment lends itself best to hospital usage In this apparatus the carbon dioxide is removed from the air by soda lime and ice is needed for the cooling system

It has been shown that subcutaneous administration of oxygen does not materially affect the oxygen content or the percentage of oxygen saturation of the arterial blood

Barach[14] has diluted oxygen with helium gas and successfully employed the mixture in patients suffering from severe asthma and in conditions associated with obstruction of the upper air passages (see Chapter 16) Helium is a lighter gas and the helium-oxygen mixture requires considerably less effort to breathe than air and oxygen

A thorough understanding of the technic of the various methods of oxygen administration is essential for success The regulation of the apparatus should never be left to an uninstructed nurse or attendant Physicians unfamiliar with the details of this method of therapy should either not employ it or else should call in consultation a colleague who understands both the errors of technic and the advantages of the procedure In arranging the patient in a tent it is well to keep in mind that the mattress is pervious to oxygen, consequently a rubber sheet should cover the mattress and the patient should be carefully tucked in if the efficiency of the method is to be maintained The tent should be of non diffusing material and should be kept in good condition at all times Leaks reduce efficiency and are expensive It is well to remember that there is only one kind of oxygen used industrial oxygen There is no special 'medical oxygen'

## TOTAL THYROIDECTOMY

Total ablation of the thyroid gland was first proposed by Blumgart and his associates[31] in 1933 as an aid in a carefully selected group of patients suffering from congestive cardiac failure or angina pectoris The scientific basis for this new form of therapy is logical and remains unassailable although the results in many cases have been disappointing

The heart has increased work to do in the presence of an elevation of the basal metabolic rate If this rate is purposely lowered to the myxedema level less work is required of a heart already showing evidence of reaching the limit of its functional capacity by the presence of congestive failure or angina The margin provided by the operation may enable the patient to be about again without recurrence of the symptoms of edema or chest pain on slight exertion Although it was a well known clinical fact that

patients with heart disease and thyrotoxicosis showed considerable cardiac improvement after subtotal thyroidectomy it remained for Blumgart and his colleagues to recommend the removal of the normal thyroid

Patients must be carefully selected not by the surgeon but by the internist only after careful study if successful results are to be obtained Operation should never be considered until a medical regime has been given a fair trial in competent hands Cases are few where digitalization and the use of one of the mercurial diuretics combined with bed rest and diet do not produce marked improvement in all the symptoms of con[illegible] gestive failure The operation is recommended for the small group [illegible] remain comfortable under appropriate therapy at bed rest but [illegible] the slightest increase in activity is allowed show prompt recurre[illegible] symptoms It must also be kept in mind that the operation that [illegible] this added amount of exercise tolerance is not without its risks [illegible] where the cardiac lesion has given evidence of its tendency [illegible] rapidly in patients with coronary arteriosclerosis syphilitic [illegible] complications or in some patients who already have a low basal [illegible] rate nothing is to be gained by attempting thyroid ablation [illegible] it is evident that the number of cases benefited by the [illegible] further decreased White[193] estimates that 1 per cent of all the [illegible] routinely seen for congestive failure or angina pectoris will [illegible] prove suitable for the procedure of total thyroidectomy

In addition to the care necessary in the selection of the [illegible] most important to obtain a surgeon experienced in the [illegible] thyroid operation if fatalities are to be reduced to a min[illegible] care of the patient calls for regulation of the myxed[illegible] medical regime of digitalis and diuretics is continued [illegible] is added if required to maintain the basal metabolic [illegible] minus 30 per cent

## FOLLOW UP TREATMENT

When the signs of congestion vanish and the patient [illegible] tory the physician's work is by no means finished [illegible] nized very quickly the signs and symptoms of cardiac [illegible] them promptly and efficiently to the great satisfaction [illegible] his family but the task is not completed until the [illegible] condition has been determined The patient's futu[illegible] intelligently planned

In some cases discovery of the etiology will [illegible] others difficult At the time of the initial exam[illegible] valuable points may have been gathered fro[illegible] example several attacks of rheumatic fever [illegible] tension or angina On examination increase in [illegible] of hyperthyroidism certain characteristic mur[illegible] pulsations bulgings or retractions of the thorax [illegible]

ing to the nature of the underlying cardiac lesion may have been discovered (Chapter 1)

When the etiologic background is established the physician is in a position to give advice in regard to the probable future course of the disease For example patients with rheumatic heart disease particularly if auricular fibrillation is present at the onset of congestive failure usually respond promptly to treatment and may show no recurrence of failure for a number of years, provided digitalis and diuretic drugs are properly administered The same may be said concerning cases of hypertension If the initial failure is regarded as a warning and co-operation obtained these patients may do very well for some time The same optimistic outlook cannot be held where syphilitic heart disease is shown to be the cause of the failure Here initial improvement may take place following the usual regime of treatment but it does not last and a poor prognosis must be given The same may be said of patients where frequent coronary occlusions have greatly reduced the myocardial reserve A small number of cases will be seen where prompt recognition of the cause of the congestive failure may result in complete restoration of circulatory function for an indefinite period (pages 182 556)

The type of patient we are dealing with many times has a definite bearing on prognosis If intelligent and co operative the outlook is improved for modern methods of management have much to offer The station in life may likewise affect the future in that the type of work to which the patient returns after the breakdown may precipitate another attack However I do not believe that complete rest for an indefinite period is the best treatment for working people The issue has often been settled for me by the patient when I have been in doubt about the ability to return to a previous occupation Of necessity the head of the house returns to mill or factory, or the housewife to her household duties and the care of her children Mild grades of congestive failure have reappeared in some cases but even so I have been surprised at what could be accomplished by these patients in spite of this handicap

The frequency of congestive failure as a cause of death in heart disease has shown a decided drop during the past decade for the newer methods of treatment enable us to keep cardiac patients edema free Williams and Rainey [403] comparing the incidence of congestive failure in patients from their files who died between 1931 and 1935 with a similar series between the years of 1926 and 1930 found that congestive failure accounted for 31 per cent of the deaths in the early group while it accounted for only 18 per cent in the 1931-1935 series Their figures in addition show that the duration of life after the onset of symptoms has in recent years been distinctly prolonged This reflects the value of the modern treatment of congestive failure

In the following cases problems of management of congestive failure will be reviewed The treatment of the etiologic types of heart disease

that are represented here has been considered under other chapter headings

## ILLUSTRATIVE CASES

### Hypertensive Cardiovascular Disease Complicated by Congestive Cardiac Failure

**Case 4** Miss E M a housekeeper of 57, was first seen 1/ 36 complaining of dyspnea edema and vomiting Four weeks before there was marked increase in dyspnea followed by edema of the feet worse toward evening She was forced to remain in bed on 1/21/36 because of dyspnea Vomiting began the same day and when examined the patient was unable to retain even fluids by mouth The past medical history was negative The family history revealed that her mother died at the age of 70 of hypertensive heart disease

Physical Examination B P 130/100 Pulse 130 Rhythm totally irregular Cyanosis and dyspnea were present The heart was enlarged to the left L B 13 6 cm R B 3 0 cm There was a blowing systolic murmur of mod rate intensity present over the mitral area The right chest posteriorly showed flatness as far as the angle of the

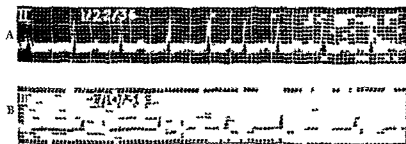


Fig 48 A Auricular fibrillation Ventricular rate 150
B Following digitalization Note the depression of the S T intervals and the greatly reduced ventricular rate

scapula The liver was enlarged 6 cm below the right costal margin No ascites Edema of the legs was present

Laboratory Data The electrocardiogram (Fig 48) showed auricular fibrillation with a rapid ventricular rate Urinalysis light cloud of albumin specific gravity 1 02 no sugar and an occasional red blood cell

Clinical Diagnosis A Etiologic Hypertension B Anatomic Cardiac hypertrophy C Physiologic Auricular fibrillation Congestive cardiac failure D Functional Classification Class 4 Therapeutic Classification Class F

*Discussion* This clinical picture is frequently encountered Although the systolic blood pressure was not elevated when the patient was first examined the diastolic level showed a suspicious increase The presence of cardiac enlargement the family history of hypertension and the age of the patient were additional factors of importance in establishing the etiologic diagnosis We may surmise from the history that early left ventricular failure was present four weeks before the patient was compelled to remain in bed Failure of both ventricles was evident when she was first examined

Treatment was begun with an injection of morphine sulfate 15 mg (¼ grain) Because of the cyanosis dyspnea, and tense jugular veins a venesection was performed and 600 cc of blood was quickly withdrawn Following this, the venous engorgement was visibly improved, and the patient felt better

Vomiting was the next problem that demanded attention No medication had been previously taken This removed the possibility of vomiting as a result of digitalis toxic action In patients showing such marked clinical evidence of venous engorgement vomiting usually arises secondary to the congestion of the entire gastro intestinal tract

Since it was impossible to give digitalis by mouth when the patient was first seen the rectal route was chosen After a cleansing enema 8 cc of digitan (equivalent to 0 75 Gm [12 grains] of the whole leaf of digitalis) were given through a tube and washed in with one ounce of tap water For the next 12 hours nothing but cracked ice in small quantities was allowed The next day the vomiting had stopped diuresis had started and the patient felt much improved Oral administration of digitalis was therefore begun and one tablet 0 1 Gm (1½ grains) of the whole leaf was given every four hours The pulse on the second day was still irregular, but the rate had dropped to 90 beats per minute A Karell diet (page 548) was prescribed and was well tolerated The vomiting did not recur

Since some edema was still present on the fourth day 1 cc of mercupurin was given intravenously and at the same time the digitalis dosage was cut to 0 1 Gm (1½ grains) twice daily inasmuch as the pulse rate had dropped to 80 The diet was increased and the fluid allowance raised to 2000 cc daily On the sixth day the pulse was 70 consequently the digitalis dose was lowered to maintenance 0 1 Gm (1½ grains) daily The blood pressure at this time was 180/100 confirming the original impression concerning the etiology This increase was not regarded as an alarming sign The blood pressure with restoration of circulatory efficiency had merely returned to its previous level

At the beginning of the second week a regular diet was prescribed and the patient was allowed to sit in a chair beside the bed There was no evidence of edema dyspnea did not reappear and the pulse rate was 75 and irregular In the presence of cardiac enlargement and congestive failure, no attempt was made to restore normal rhythm Auricular fibrillation was accepted and the ventricular rate controlled by maintenance doses of digitalis These patients rheumatic or hypertensive get along better with an established fibrillation than they do if attempts are made to restore co-ordinated auricular contractions Restoration of sinus rhythm by quinidine materially increases the possibilities of embolism from clots that may be swept away from the auricular walls

Three weeks later this patient was able to carry out lighter duties of the household The heavier work that had been largely responsible for precipitating the attack of congestive failure was turned over to a part

time maid Rest periods were continued in the afternoon The patient was permitted to take short walks on the level out-of doors on clear days and social activities were encouraged Since she enjoyed sewing and was skilled in certain types of needlework she managed in time to obtain enough work from her neighbors to pay for the services of the maid

### Hypertensive Cardiovascular Disease Congestive Failure and Cardiac Asthma in a Patient Abnormally Sensitive to Digitalis and Morphine

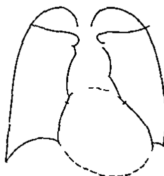
**Case 5** Mrs R M an American housewife of 53 was first seen in January 1937 complaining of severe chest pain Previously she had received treatment over the course of five years for hypertension The main symptoms complained of during this time were vertigo and palpitation ( skipping of the heart )

Physical Examination When the first examination was made severe chest pain had been present for 4 hours requiring two hypodermic injections of morphine for relief Nevertheless her condition was excellent B P 170/100 T 98 F The pulse was 80 and regular The skin was warm and dry and the color was good An electrocardiogram showed no evidence of coronary occlusion The cause of the chest pain was evident the next morning when a typical herpetic eruption appeared (Fig 49B)

A subsequent study showed that the heart was enlarged to the left (Fig 49A) Systolic murmurs were present over the mitral and aortic areas The aortic second sound was accentuated An electrocardiogram showed frequent premature beats (Fig 49C) and alterations in the T waves consistent with the diagnosis of hypertensive heart disease The blood Wassermann reaction was negative Several blood counts and urinalyses showed no departure from the normal

Clinical Diagnosis A Etiologic Hypertension B Anatomic Cardiac hypertrophy Relative mitral insufficiency C Physiologic Frequent premature ventricular contractions D Functional Classification Class 1 Therapeutic Classification Class C

**Discussion** Before the appearance of the skin eruption a diagnosis of acute coronary occlusion had been made This alarmed the patient and the pain that persisted following the healing of the eruption also contributed to a rapid down hill course When re examined three months later the heart was found to be increased in size and dyspnea was present on less exertion Two months later when evening edema began to appear digitalis was prescribed The first dose of the drug consisted of a tablet 0 1 Gm (1½ grains) of the whole leaf This was promptly vomited Repetition of half the dose two days later had the same effect A week later the drug was again administered disguised in a colored capsule This time the vomiting lasted two days and the edema and dyspnea increased to such an extent that bed rest became necessary A capsule containing phenobarbital 30 mg (½ grain) and theobromine sodium acetate 0 3 Gm (5 grains) given after meals was well tolerated At the end of a week of complete bed rest the first typical attack of cardiac asthma occurred Although a hypodermic injection of morphine sulfate 15 mg (¼ grain) brought prompt relief it was followed by a severe vomiting that continued for two days When this was controlled attacks of nocturnal dyspnea again returned and were more severe The patient s condition during one of these attacks made the use of morphine again a necessity Vomiting promptly reappeared and the usual measures including gastric lavage were entirely ineffectual in lessening its severity

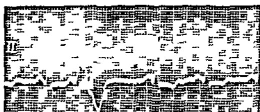


A



B







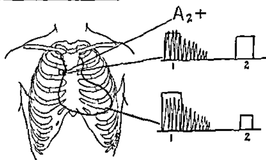
C

FIG 49 A The orthodiagram Note cardiac enlargement (chiefly left ventricular) The right upper cardiac border is formed by the ascending arch Systolic pulsations were visible in this region

B The appearance of the precordial region two days after the onset of chest pain

C The electrocardiogram *Note frequent ventricular premature beats* The voltage of the QRS groups is increased T is diphasic and T 3 is flat Left *axis deviation is present*

D Diagram representing clinical findings




D

However the large amount of fluid lost in the vomitus, in addition to the greatly restricted intake during this period appeared to decrease the frequency of the attacks of cardiac asthma Consequently although no edema was visible on physical examination injections of mercupurin were tried Following a satisfactory response to 1 cc intravenously the amount was increased to 2 cc with excellent results Attacks of cardiac asthma did not recur after mercupurin injections were begun

A series of 62 injections of mercupurin have now been given during the past 18 months Although the patient has been confined to her room by the greatly diminished cardiac reserve she has been entirely comfortable and free of paroxysmal dyspnea The only additional medication given during this period has been *ammonium* chloride in enteric coated pills 1 0 Gm (15 grains) after meals and a capsule of phenobarbital 60 mg (1 grain) at night No untoward effects of the mercupurin have been observed The cardiac signs during this time have remained unchanged The rhythm has been more regular and a ventricular rate of 80 has been maintained

This patient is a good example of the progress that has been made in recent years in the treatment of congestive failure In some cases control of the fluid balance of the body through the use of the organic mercurial preparations gives relief even though the accumulation of edema fluid is not evident on clinical examination Future studies are awaited to reveal the mechanism involved in this process

### Syphilitic Heart Disease—Sudden Death During First Attack of Congestive Failure—Autopsy

**Case 6** F R a colored laborer of 40 was admitted to the Philadelphia General Hosp tal on 5/4/26 The chief compla nts were shortness of breath and swelling of the legs and abdomen The pat ent dated the onset of his illness four months before admission when dyspnea on exertion first appeared This increased and was followed by cough Hemoptysis was present on three occasions S x weeks before admission edema of the feet w s noted in the evening It gradually became more marked involving the thighs and finally the abdomen The dyspnea had increased to orthopnea on admiss on Th patient gav a history of chancre at the age of 5 for hich no treatment had b en received

Physical Examination B P 188/ 8 Orthopnea Anasarca D st ntion of neck veins Pulsating arter es in neck and ar ns The apex beat was in the fifth interspace in the anterior ax llary line Systolic and d astolic thrills were palpable in the third and fourth interspac s 1 5 cm to the left of the sternal margin Th first sound of the heart heard over the apex was accentuated The aortic second sound was absent and was replaced by a long loud diastolic murmur A loud systolic murmur was heard over the aortic area transmitted to the arteri s of the ne k Over the third and fourth left inter spaces there was a loud rasping murmur The abdomen was tense and a flu d wave was present A pi tol shot sound w s heard o er both femorals

Laboratory Data Wassermann four plus Blood urea n trogen 75 mg per cent The u ine reveale l a fa nt trace of albumin The electrocardiogram showed no abnormality except a left axis deviatior Th roentgen ex minat on showed cardiac enlargement with aortic configuration There was no sign of aneurysm

Diagnosis A Etiologic Syph l s B Anatomic Cardiac enlargement Aort c regurgitat on Aortitis An urysm (?) C Physiol gic Normal s nus rhythm Con estive ardiac failure D Functional Class ficat on Class 4 Therapeutic Classification Class E

A



B

Fig 50 Syphilitic cardiovascular disease

A Increased cupping of the aortic leaflets is present A sacculation appears behind the anterior leaflet At this site an aneurysm projects into the pulmonary artery

B The Pulmonary Artery The point of rupture of the aneurysmal sac is seen Note the area of thickening on the wall opposite point of rupture (Autopsy No 17 193 Philadelphia General Hospital)

Course The patient failed to show any improvement following digitalis and diuretic therapy and died suddenly on the third hospital day

Autopsy Marked cardiac enlargement and dilatation were found (Fig 50A) There was increased cupping of all the aortic leaflets The anterior leaflet showed a more marked change with sacculation to the size of a marble in the lower half The base of this sac was ruptured The adjacent tissue of the aortic leaflet was sacculated to the size of a pigeon egg and projected into the pulmonary artery (Fig 50B) The wall of the pulmonary artery opposite the perforation as roughened probably the result of the blood gushing through the opening In the anterior wall of the descending portion of the aorta there was a small sacculated aneurysm containing a moderate amount of laminated clot

Discussion The treatment of cardiac failure following syphilitic cardiovascular disease does not differ from that recommended in other types The prognosis however is far more serious in syphilis when symptoms develop to the extent that were observed in this patient on admission Survival of the rheumatic or hypertensive patient for some time following one or more episodes of congestive failure is not unusual On the other hand while a fairly good state of health may be maintained by the patient who has syphilitic aortic regurgitation when signs of circulatory failure can be detected clinically the end of the road is not distant Sudden death may be expected however at any point in the course of the disease Valvular or aneurysmal dilatations with subsequent rupture and the establishment of an intrathoracic arteriovenous aneurysm may precipitate the terminal episode of congestive failure in some instances as demonstrated in this case

Intravenous arsenical preparations are contraindicated in the management of these patients while the heavy metals should be withheld until the evidences of congestive failure disappear This patient received no treatment either for his syphilis or his cardiac condition until three days before death When he entered the hospital the prognosis was hopeless Earlier recognition of the cardiac involvement followed by intensive specific treatment would undoubtedly have delayed the onset of congestive failure many years

## Rheumatic Heart Disease—Stenosis and Regurgitation at All Valvular Orifices—Congestive Failure of Exceptionally Long Duration

Case 7 Mrs B K a housewife of 49 when first examined in June 1933 presented the typical picture of congestive failure Circulatory symptoms had appeared four years prior to the initial examination and the patient had been admitted on three occasions to local hospitals for treatment of congestive failure There was a history of three attacks of rheumatic fever in childhood

Physical examination showed a thin adult female sitting up in bed There was a trace of icterus The jugulars were turgid (Fig 51D) Orthopnea was present Inspiratory rales were heard over both lung bases The heart was enlarged to percussion The left border was readily detected in the anterior axillary line and the right border was percussed 6 cm to the right of the mid sternal line Systolic thrills were palpable over the aortic pulmonic and mitral valve areas The sounds at the base were replaced by loud systolic and diastolic murmurs Presystolic and diastolic murmurs were heard over the mitral area Separate murmurs were not distinguishable over the tricuspid area Ascites was present (Fig 51C) as well as edema of both feet

LABORATORY DATA The electrocardiogram showed the presence of auricular fibrillation (Fig 51B) The roentgen ray study (Fig 51A) showed enlargement of all chambers of the heart Increased hilum markings were seen but there was no evidence of pleural thickening or effusion Evidence was present of some calcium in the pericardium but fluoroscopically there was good differentiation between auricular and ventricular impulse

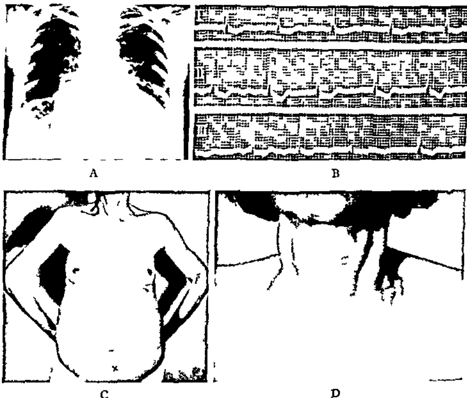


FIG 51 A Roentgenogram showing cardiac enlargement in all diameters
B The electrocardiogram Auricular fibrillation is present Note the depression of the S T Intervals in all leads caused by digitalis action
C Marked ascites
D Swollen jugular veins Patient in erect position

indicating the absence of pericardial effusion Urinalysis and blood count were normal The blood Wassermann reaction was negative

CLINICAL DIAGNOSIS A Etiologic Rheumatic Inactive B Anatomic Cardiac enlargement Mitral aortic *tricuspid and pulmonic stenosis and regurgitation* C *Physiologic* Auricular fibrillation Congestive cardiac failure D Functional Classification Class 4 Therapeutic Classification Class E

DISCUSSION Murmurs and thrills typical of stenosis and regurgitation were elicited over the aortic, mitral and pulmonic areas The findings were not so distinct over the tricuspid area However in the presence of such an extensive rheumatic endocarditis it is reasonable to suppose that the tricuspid valve was involved at least to some degree in the same process The presence of ascites and other signs of venous congestion

gave further support to the diagnosis of tricuspid stenosis Other conditions that might account for the same clinical picture are chronic adhesive pericarditis (page 181), or a massive pericardial effusion Adhesions in the region of the inferior vena cava or at the base of the right lung might obstruct the venous flow with the same result The roentgen study was useful in ruling out these possibilities

When this patient was first seen she was given a hypodermic injection of morphine 15 mg (¼ grain) and digitalized in the usual manner Following the intravenous administration of 1 cc of mercupurin the next day, there was a diuresis amounting to 6000 cc The edema of the feet disappeared completely, and the dyspnea was greatly relieved The ascitic fluid collection was unaffected and two days later 10 000 cc of a clear amber fluid were removed from the abdomen (page 95) Following this procedure the liver was readily palpable a hand s breadth below the right costal margin It was smooth firm and slightly tender

Intravenous injection of 2 cc of mercupurin was begun and continued every five days in an attempt to prevent the reaccumulation of ascites Although the fluid collected in the peritoneal cavity the amount was much less than ordinarily observed and some decrease in the abdominal tension followed each injection of the diuretic During the first few months nausea and occasional vomiting spells appeared the day after the injection of the mercupurin A pulsus bigeminus was observed at this time These signs and symptoms suggested a toxic action following the diuresis which swept back into the blood stream the digitalis contained in the body fluids The maintenance dose of digitalis was accordingly stopped the day before the injections of mercupurin and resumed the following day The toxic effect did not reappear The pulse remained at 70 the appetite improved, and the exercise tolerance was fair A mild state of congestive failure persisted but the patient was able to be about on one floor of the house

During the next six years a total of 430 injections of 2 cc of mercupurin at five day intervals were given to this patient Repetition of the abdominal tapping was unnecessary for four years Paracentesis was performed once during the fifth year and three times during the sixth year The patient is still ambulatory at this writing She has been most co-operative in keeping her intake-output records and is an expert in the matter of digitalis maintenance dosage She illustrates what may at times be accomplished by maintaining digitalis plus maintenance diuretic therapy

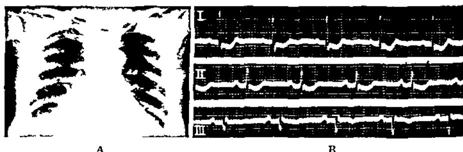
Long periods of survival from the time of onset of symptoms of congestive failure are not uncommon in these patients who show combined valvular lesions The continued congestion of the portal system in this case that followed the development of tricuspid stenosis may serve a useful purpose in limiting the return flow of blood to the heart and relieving the strain on a badly damaged organ For the same reason the pulmonary fields show a less marked congestion than is usually found in

patients with mitral stenosis alone Since the left auricle of this patient was greatly dilated it is reasonable to suppose that the mitral stenosis took place first and was followed by the tricuspid lesion at the time of a subsequent attack of rheumatic infection

### Sudden Left Ventricular Failure with Cardiac Asthma in a Patient with a Past History of Bronchial Asthma—Differential *Diagnosis* and Management

**Case 8** Mrs L A a housewife of [illegible]0 was first seen in May 1939 during an attack of "asthma The countenance was ashen the lips blue and the skin cold and damp Dyspnea of the asthmatic type was extreme and there were numerous bubbling rales in both lungs and a frothy blood tinged expectoration

Physical Examination B P 1[illegible]0/90 The left cardiac border was percussed in the axilla No edema of the extremities was present The liver edge was barely palpable *The past history was negative except for the presence of attacks of* asthma *for* [illegible]0 *years* However the usual methods had been unsuccessful in giving relief in the present seizure For this reason the patient was brought to the hospital




A B

Fig 5 A The roentgenogram shows considerable cardiac enlargement Note calcification of the aorta and the obliteration of the right diaphragmatic angle
B The electrocardiogram shows a deep Q wave in lead 3 and a left axis deviation The S-T Intervals in leads 1 and 2 are depressed (digitalis action)

Clinical Diagnosis A Etiologic Hypertension Arteriosclerosis B Anatomic Cardiac hypertrophy C *Physiologic Normal sinus rhythm Paroxysmal cardiac dyspnea or cardiac asthma* D Functional Classification Class 3 Therapeutic Classification Class E

**Discussion** The diagnosis of allergic asthma in a patient of this age even in the presence of a history of attacks of asthma for 20 years is risky However if allergic asthma develops late in life (which rarely happens) *it may simulate heart disease* and the attacks may be no different clinically from those observed in patients who have cardiac asthma On the other hand a patient who has had allergic or bronchial asthma for some years may also develop hypertension Hypertrophy of the left ventricle may progress asymptomatically until sudden failure occurs with the production of a more severe type of asthmatic seizure[38] (Chapter 16)

The age the appearance and the size of the heart of the patient under discussion suggested cardiac asthma Likewise the response to rest vene

section and morphine was prompt In other instances however the diagnosis is by no means so easily made

The response to epinephrine in a patient giving a previous history of allergy may be confusing In this case epinephrine had given but slight relief compared to the marked benefit that always followed its administration in previous years Untoward effects on the other hand are not at all uncommon following the persistent use of epinephrine in this type of heart failure

The clinical examination often gives the most valuable evidence for making the differential diagnosis Fortunately in this patient although emphysema was present to some degree accurate determination of the heart size was possible The accentuation of the pulmonic second sound also attracted attention to the congested condition of the pulmonary fields secondary to the sudden failure of the left ventricle In patients who exhibit less pronounced signs of cardiac disease other diagnostic measures are necessary

Venous pressure readings have been useful in differentiating bronchial from cardiac asthma During an asthmatic seizure of purely allergic origin the venous pressure is usually normal while marked elevation may appear in the presence of the left ventricular failure that accompanies cardiac asthma During a paroxysm however the technic of the procedure is not as readily carried out as it is after the attack has been relieved

For this reason estimation of the circulation time is now looked upon as the most valuable laboratory procedure in making the differential diagnosis During an attack of left ventricular failure the velocity of the blood flow through the lungs as well as in the systemic circulation is decreased The cyanide method is probably the best to use because of the sharp end point obtained that does not depend on the response of the patient Arm to lung time may likewise be satisfactorily measured by the injection of 0 3 cc of ether into the arm vein and noting the time that elapses before it is detected on the patient s breath The patient with uncomplicated bronchial asthma will show normal circulation time while cardiac asthma produces an increase in the circulation time [160 401 318]

This patient was slowly digitalized after relief of the attack was obtained The whole leaf of digitalis was used and full effect was observed when 15 tablets (0 1 Gm each) had been given over the course of a week At the end of this time the patient felt much improved and since there had been no recurrence of the paroxysmal dyspnea she was anxious to go home Two days following discharge however mild seizures began to appear at night and for the first time a slight amount of edema of the feet was noticed The liver was 5 cm below the right costal margin Consequently she was given two enteric coated tablets of ammonium chloride 0 5 Gm (7½ grains) after meals and injections of mercupurin (2 cc ) every sixth day A maintenance dose of digitalis found to be 1½ grains every second day was continued and 60 mg (1 grain) of

phenobarbital was given at bedtime Although the patient was allowed to be out of bed her activities were restricted to one floor of the house, and she was advised to create a part time position in her household for a willing but much younger neighbor On this program she has had no recurrence of her attacks of cardiac dyspnea for a period of five months

Although a good therapeutic result was obtained considering the age and the amount of cardiac damage present the one mistake in management was made when the patient was permitted to be out of bed and to return home in one week This no doubt, was responsible for recurrence of the attacks A minimum period of three weeks away from even the lighter burdens that arise in the care of a home should be obtained If thrombi have formed in the heart during the period of congestive failure when slowing of the blood stream takes place the prolonged rest period may permit them to become better organized and adherent and consequently there may be less subsequent danger of embolism The longer rest may also be a factor in preventing early recurrence of attacks of congestive failure since it makes possible a more complete training in proper regulation of the regime and allows a better recovery of the cardiac muscle

A patient may occasionally be encountered where the etiology of the congestive failure is obscure If a malignant growth has been discovered in any part of the body, a metastatic process involving the heart should be suspected (page 430)

Edema resulting from vitamin B deficiency states may likewise appear in rare instances in the guise of cardiac failure It may be entirely due to the lack of the vitamin or the vitamin deficiency may be the contributing cause in the appearance of symptoms in a patient with previous cardiac damage Consequently when the etiology of congestive failure is obscure inquiry should be made concerning the dietary habits (page 556)

# 3

# THE PROBLEM OF RHEUMATIC HEART DISEASE

When climatic conditions have augmented the severity of a disease or epidemic the customary therapeutic measures are much less efficacious than a change from the predisposing climatic conditions —CORVISART 1806

Rheumatic infection is the most frequent cause of organic heart disease Appearing in variou guises it bewilders us when we become too optimistic concerning our progress in the conquest of infections While perhaps not the most fatal the rheumatic state is one of the most crippling of the diseases that attack mankind Although referred to by some as acute articular rheumatism we can say as we view this infection in the light of modern knowledge that it is neither entirely acute nor entirely articular It now seems certain that once invaded the human host may harbor the inciting agent for months or years and when resistance is lowered acute exacerbations may appear In this respect rheumatic infection is not unlike tuberculosis and syphilis

The rheumatic invasion is not always accompanied by articular manifestations in fact in some instances the disease may be present for years and never produce joint symptoms or for that matter rheumatic pains of any kind As more detailed knowledge is accumulated the real nature of rheumatic disease has been recognized and today instead of considering this modern plague of childhood as an acute disease limited to one region of the body we regard it as a chronic smoldering threat to the integrity of many organs Although much attention centers around the results of rheumatic invasion of the heart few organs of the body fail to feel its touch or lack in a few years the typical scars that reveal its presence The fibrous tissue structures in the body bear the main burden of the attack The heart the joints the subcutaneous tissues the lungs the brain and other organs all show inflammatory reactions that involve this element of their structure

The clinical picture produced by rheumatic infection is by no means uniform In children as a rule the cutaneous tissues are involved to a greater extent than the joint structures However the signs and symptoms may vary even in individuals of the same group One child may have chorea another tonsillitis a third only fever and loss of weight and yet the same amount of heart damage may result in each case

## PRESENT DAY VIEWS ON ETIOLOGY

Although the search has been long and intense the cause of rheumatic fever or the rheumatic state is still a matter of controversy Numerous investigators have isolated streptococci from the lesions, but proof that *these organisms have a direct relationship to rheumatic fever has not been* convincing As early as 1900 Poynton and Paine demonstrated the presence of a diplococcus in the blood and tissues of rheumatic patients Many subsequent investigators have confirmed this observation while others have held out against a too quick acceptance of the streptococcus as the specific cause of the rheumatic process *Shick in 1912* suggested that allergy to the toxin of the streptococcus could account for some of the arthritic and endocardial manifestations of the disease while Schlesinger and his coworkers have considered a filterable virus as the likely cause[3 9] Even protozoa have not been above suspicion as causative agents in rheumatism However while conclusive proof in the matter has yet to be presented a poll of opinions of bacteriologists at the present time would show that the streptococcus leads the list of suspected organisms

**The exact mode of entry** of the causative agent into the body is another unsettled *point Available evidence seems to point* to the tonsillar area as the most likely spot for the invasion to begin since many times initial attacks as well as recurrences are ushered in by the appearance of sore throat Cultures from the tonsillar area during acute attacks often reveal the suspected streptococcus Adenoid tissues and lymph follicles in the pharynx *as well* as decayed or abscessed teeth infected sinuses middle ear disease and the vast area of the gastro intestinal tract have been regarded as possible foci

**Age of Onset** We generally consider rheumatic infection as a disease of childhood or adolescence since in most cases the first symptoms appear between the ages of four and fifteen When the onset is observed in early adult life there are usually differences in the character the manifestations the course and the prognosis In general the earlier the onset the greater the number of recurrences and the greater the chance for cardiac involve*ment Females are affected more often than males Wilson and his co* workers[41] in a study of 400 cases of rheumatic infection varying in age from infancy to 22 years found that 61 2 per cent were females and 38 8 per cent males

**Racial Factors** A study of the various races represented in our groups of clinic patients with rheumatic heart disease is misleading since we cannot separate the racial factors from the environmental Beyond a doubt rheumatic infection is widely distributed all over the world and has been observed to attack every race of mankind However, the incidence has been reported to be much less among Chinese

**Disease of Temperate Zone** Rheumatic infection is a disease that

flourishes in temperate climates a fact that should always warrant consideration in the management of these cases Competent observers in tropical climates have repeatedly stated that they have never seen a case of rheumatic fever chorea or mitral stenosis Cold damp temperate climates favor the rheumatic state and in the cardiac clinics situated in large cities along our northern seaboard the bulk of the cases belong to the rheumatic group Acute recurrences are most common among this group in the late winter and early spring months [7, 8, 79, 80]

**Familial Incidence** Rheumatic infection has a tendency to show a much higher incidence in certain families [3] It is not at all uncommon to find a mother and one or two children showing signs of rheumatic heart disease and in some instances the lesions discovered may be identical The practitioner of the old school who acquired his patients at birth and took care of them during the years that followed fully appreciated this tendency for certain types of disease to appear more frequently in some families than coincidence could explain This keen insight often places the general practitioner above the level of the specialist in his ability to detect early manifestations of rheumatic disease and the secret of this skill lies in what we refer to today as hereditary diathesis or to state it his way *some* families offer better soil for rheumatic infection than others

**Environmental influences** cannot be entirely removed from the picture for is it not possible that the rheumatic disease arises from close contacts in families schools or barracks [1, 8] On this basis we can also explain its greater frequency in the crowded tenement districts than in the other communities where standards of living are higher Statistics show that rheumatic infection is much more prevalent in cities and towns particularly in crowded industrial sections where it flourishes *among the undernourished* children of the working classes [9, 11]

## THE LESION

Rheumatic infection produces a characteristic lesion in many of the tissues of the body We may consider this rheumatic nodule *or Aschoff* body analogous to the miliary nodule that is so common in tuberculosis As it appears in the heart muscle the heart valves the pericardium the brain and the joints it is an example of the proliferative type of tissue reaction The second type of lesion so commonly produced by rheumatic invasion is described as exudative This is found in joints and in the *pericardium* The Aschoff cells that are observed in the proliferative type are large endotheloid cells containing several nuclei They are usually surrounded by lymphocytes and plasma cell and close inspection shows a fibroblastic reaction in the surrounding tissues Aschoff bodies vary in size and shape and are most often situated near a blood vessel (Fig 53)

**The subcutaneous nodule** visible on gross inspection and *so characteristic of* rheumatic disease is similar in its construction to the Aschoff

body (Fig 54) These nodules are generally painless and may be found in some cases around the malleoli the elbows the knees or vertebral

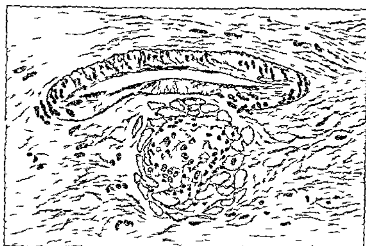


Fig 53 A typical Aschoff body Note relationship to blood vessel

spines Both of these manifestations of the rheumatic state one occurring in the myocardium as the Aschoff body of submiliary size and the other visible macroscopically in the subcutaneous tissues may appear and disappear very quickly Furthermore they may be present in abundance during some years in all rheumatic cases while during other years workers in the same clinic will detect very few This is particularly true of the nodules

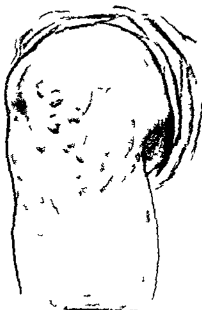


Fig 54 Rheumatic nodules

**Typical Aschoff bodies** are found at autopsy *in many*, but by no means all cases of rheumatic fever They are more apt to be present in the myocardium especially *in the auricular wall and in the interventricular septum* and usually heal with the production of small myocardial scars Occasionally in severe cases the coronary arteries become involved causing alterations in *the blood flow to the heart muscle* and consequently grave myocardial impairment may result The Aschoff bodies in the septum involve the bundle of His, and the edema that attends the inflammatory process may cause a delay in the transmission of the con

traction impulse from the auricle to the ventricle This will be reflected in the electrocardiogram (page 616) When the acute rheumatic invasion subsides, normal function of the bundle is restored (page 139)

## PATHOLOGY

Rheumatic infection reaches the heart valves through the blood stream Since the mitral valve contains more blood vessels than the others, it is usually the first to be invaded The small vessels in the valves persist longest in the mitral valve Therefore the younger the patient the greater the likelihood of rheumatic involvement In the healing process that follows the delicate texture of the valve is destroyed and it becomes thickened and stiffened Calcium deposits may occur later in these diseased tissues causing them to stand out in the blood stream increasing the obstructive or stenotic nature of the process An equally important feature of rheumatic infection as far as valvular function is concerned is the invasion and subsequent contraction of the chordae tendinae

**The inflammatory changes** produced by the rheumatic process in all severe cases spread readily to the pericardial surfaces The gloss that normally characterizes this epithelial structure quickly disappears and is replaced by a fibrinous exudate The pericardial layers become adherent and when separated at autopsy the typical 'bread and butter appearance is seen Fluid usually accompanies these exudative reactions and accumulates in the pericardial sac in small amounts

**Relation of Structural Changes to Physical Signs** Invasion of the myocardium endocardium and pericardium produces the structural alterations just reviewed These form the basis for the physical signs that we search for in patients suspected of harboring rheumatic infection Various murmurs that have been described previously (page 17) are produced the most common of course, is the one that accompanies mitral regurgitation The stiffening and thickening of the mitral valve causes the presystolic murmur of stenosis at the time of auricular systole which is best heard over the region of the apex beat while weakening of the muscular ring figures largely in the production of the regurgitant murmur When the aortic cusps are invaded insufficiency is produced, and a diastolic murmur appears which is best heard along the left sternal border In rheumatic disease at this area valvular damage is the chief factor in the regurgitation In syphilitic disease regurgitation results when the aortic wall becomes weakened and dilated and when the valve insertions in this area are included in the mass of inflammatory tissue

Invasion of the pericardium with the deposition of fibrin produces a friction rub (page 165) Later adhesions form If the layers of the pericardium become adherent little harm results and no characteristic signs appear However if the thickening of the pericardium takes place and interferes with diastolic filling of the heart much disability may result during the ensuing years (page 179)

CONSIDERABLE MYOCARDIAL DAMAGE may quickly follow acute rheumatic infection and dilatation and failure may take place early. Inflammatory lesions in the myocardium near the conduction bundle or its branches may make their presence known by functional alterations. Focal myocardial lesions may likewise produce changes in the heart rhythm by initiating premature auricular or ventricular beats.

**Other organs of the body** may be extensively involved in the spread of the rheumatic infection. Changes in the brain produce the symptoms of chorea and when the lungs are invaded the characteristic hemorrhagic manifestations that often appear have been termed "rheumatic pneumonia." Vascular lesions in the aorta as well as in the small arteries of the body are often encountered. Although the damage in the aorta may resemble that produced by syphilis in type, it cannot approach it in severity; consequently mycotic aneurysms following acute rheumatic infection, while possible, are rare occurrences.

In each patient the extent and severity of the rheumatic involvement will be different. Even when the damage is confined to the heart one patient may have a greater degree of myocardial damage with endocarditis and present many signs that can be readily detected clinically, while another may have an invasion of the myocardium that will produce few clinical signs and those demonstrable with great difficulty, if at all, in the early stages.

## SIGNS AND SYMPTOMS

The most valuable signs and symptoms to elicit in cases of rheumatic infection are those produced by activity of the process, for these guide us in the management of the patient. This is particularly true in childhood when the symptoms of the disease often simulate a tuberculous infection.

**Loss of Weight.** Activity of the rheumatic process is usually attended by loss of weight, although it is not as extreme as in tuberculosis. Many cases simply do not gain and return to the physician month after month registering the initial weight. Very few are overweight. Coombs claims that malnutrition is not so definite when aortic lesions predominate.[71, 7] He attributes the failure to gain weight to the interference with oxygenation of the tissues that is present in mitral stenosis and points to the fact that when this lesion develops early in life grave interference with development may take place (mitral dwarfism).

**Pallor** is usually present, and its appearance should always suggest activity of the rheumatic process. It may be accompanied by a moderate secondary anemia, and when mitral obstruction is present by a trace of cyanosis as well. Marked pallor of a characteristic type is seen in these patients when subacute bacterial endocarditis develops.

**Fever** usually attends the course of the disease, but its absence should not be considered as a strong point against the diagnosis of an active rheumatic lesion in the presence of other constitutional symptoms. The

elevation of the temperature may be very slight and in some cases this may be the only evidence of activity on physical examination High temperatures usually accompany fulminating infections particularly when the brain is the seat of widespread involvement

**Anorexia** In the presence of even slight fever anorexia will appear, the child will show a disinclination to play and will tire easily Irritability and nervousness are common symptoms The first visit to the physician is often made at this stage A careful examination of the run down child may then permit an early diagnosis of rheumatic infection (page 169) Many of these patients are sent to the hospital for tonsillectomy with no other symptoms than pallor anorexia and failure to gain weight A careful study of every child should be carried out before operation since an ill advised tonsillectomy at this stage usually gives a considerable impetus to the invasion

**A sore throat** heralds the onset of a rheumatic exacerbation in many instances, but is not invariably present All types of muscle and joint pains in children should be viewed with suspicion and a thorough investigation should be made The importance of joint pains is emphasized when they occur with any other of the manifestations of rheumatic disease The joint pain may be a mild evanescent process in some cases while in others one joint after another may be attacked in typical textbook fashion usually the wrists ankles knees elbows and shoulders in the order named the pain and swelling disappearing from one joint as another is attacked

**The nervous child** should be examined to rule out rheumatic infection Children sent home from school because of their inability to sit still should be disciplined only after a visit has been made to the physician The twitchings and choreiform movements become pronounced and generalized when the infection in the nervous system has advanced Choreiform movements are accentuated by excitement and activity and are usually absent during sleep Although rheumatic infection is by far the most common type of involvement causing chorea other diseases for example syphilis and encephalitis may occasionally produce it

**Symptoms of a pulmonary nature** may occur in many cases, these have suggested to some investigators a special type of rheumatic pneumonia Specific lesions in the lungs have been described[137, 39, 46] but here there is much difference of opinion Hemorrhagic manifestations should not puzzle the physician when they occur during the course of acute rheumatic fever When they select the lungs and many alveoli are involved they produce physical signs that simulate pneumonia[393]

**Abdominal Pain** During the course of rheumatic fever particularly in children attacks of abdominal pain are not infrequent In some cases this symptom may be referred from a pericardial lesion In others the pain may be related to the gastric disturbance that sometimes attends salicylate medication In some children suffering from acute rheumatic infection unexplained vomiting may occur Rarely lesions of a rheumatic nature involving the hip joint may cause abdominal pain

**Invasion of the heart** during the course of rheumatic fever may be heralded by an increase in the temperature and an elevation of the pulse rate When the pericardial sac is involved precordial pain may appear It is sharp, increased by breathing and by pressure of the stethoscope over the heart area and is usually accompanied by the characteristic to and fro friction sound In some instances the friction rub is present without pain A dull aching variety of precordial pain may occur at times in the absence of pericarditis Pain of the anginal type is very rare following rheumatic infection except in the presence of aortic valvular disease with regurgitation when it is usually believed to be a result of the low diastolic pressure and the decreased coronary filling I have seen only two rheumatic children who had anginal pain associated with an aortic regurgitant lesion

PALPITATION occurs and may be part of an effort syndrome that not infrequently accompanies any infectious process or it may be the result of the presence of frequent premature beats Only rarely is it caused by paroxysms of tachycardia or auricular fibrillation

DYSPNEA frequently accompanies an acute rheumatic carditis in children and is generally attended by cardiac dilatation It may be accentuated by the collection of fluid in the pericardial sac Very seldom is the fluid present in sufficient amount following rheumatic infection to cause symptoms of tamponade and to require tapping (page 164) Dyspnea is one of the most common symptoms of chronic rheumatic heart disease usually increasing as the lesion develops

**Hemorrhagic episodes** are characteristic features of rheumatic disease consequently an unexplained nose bleed in a child particularly if recurrent is a suggestive symptom Purpura may be a rheumatic manifestation in rare cases although even when associated with joint pains such evidence is by no means conclusive Embolic phenomena secondary to the endocardial involvement in acute rheumatic fever are rare

**Physical Examination** Detecting the presence of a disease that attacks nearly all the structures of the body containing fibrous tissue calls for a complete physical examination not merely a cardiac study The color of the skin and mucous membranes should be noted Since petechiae nodules and skin rashes are important in diagnosis the patient should be stripped Careful observations should be made before during and after the examination for the presence of twitchings Nose throat ears sinuses teeth and pharynx should be inspected for evidence of infection The lymph nodes draining these areas should be carefully palpated and roentgen examinations made when indicated

CARDIAC EXAMINATION generally reveals little in the early stages In some instances the only signs aside from the tachycardia may be furnished by an electrocardiographic study Here prolongation of the conduction time (pages 615 139) may point to an acute rheumatic carditis Signs of organic valve lesions are not present early in the disease If signs of pericarditis are present usually they have been preceded by more easily recognizable signs of cardiac involvement Enlargement of the heart may

be evident on percussion and it may be accompanied by the systolic apical murmur of relative mitral insufficiency This soft murmur is usually the first on the scene and the question always arises as to its exact significance That it may at times be functional is shown by its disappearance when the acute infection subsides and the reappearance later of a murmur of harsher pitch which is more significant evidence of organic valvular involvement

VALVULAR LESIONS In the later course of the rheumatic disease valvular lesions offer abundant evidence of the presence of a cardiac invasion in fact so absorbed does the student become in their study that other signs are often unrecognized Mitral valve disease is most frequent and the



FIG 55 Rheumatic heart disease Stenosis of the mitral valve viewed from above

harsh systolic apical murmur of uncomplicated regurgitation is more common in children It is attended by an accentuated pulmonic second sound and cardiac enlargement With recurring infection or with increased contraction of the scar tissue in the valve following the initial invasion stenosis develops The first reliable sign of its presence is a mid-diastolic apical murmur To elicit the signs of early mitral stenosis the patient should always be examined in both the erect and recumbent positions Many times a murmur that is inaudible or questionable in the erect position becomes clearly evident in recumbency after exercise particularly if the patient is examined lying on the left side Later in the course of the disease the diastolic murmur may be readily heard in the erect position, and the typical presystolic accentuation will be recognized As the stenosis of the mitral valve advances (Fig 55), the first heart sound at the apex becomes louder and acquires a decided slapping quality Palpation over the area of the apex will now reveal a diastolic thrill Definite alteration in the cardiac silhouette occurs when mitral stenosis becomes established (Figs

20 21) and characteristic changes may also appear in the electrocardiogram (See Fig 190)

In advanced mitral stenosis the left auricle becomes dilated Further weakening of its walls by the inflammatory process that accompanies the rheumatic state makes it a vulnerable spot and sooner or later auricular fibrillation replaces normal rhythm (page 145) When co ordinated auricular contractions cease the crescendo quality of the apical diastolic murmur disappears and only a short murmur is heard in this area in early diastole The diagnosis of stenosis will then depend on the other features of the case, particularly the quality of the first heart sound and the appearance of auricular fibrillation in a patient with a definite rheumatic history

When rheumatic infection attacks the aortic valve the same changes occur and result first in regurgitation and later in stenosis No sign of involvement of the aortic valve appears on physical examination until a cicatricial retraction produces regurgitation As a portion of the blood projected into the aorta during systole flows backward through the damaged valve into the ventricle in diastole it produces a blowing murmur heard best along the left sternal border at the third or fourth interspace The murmur of aortic regurgitation may be heard at the end of expiration with the patient in the upright position and bending forward Faint diastolic murmurs of early aortic regurgitation may sometimes be detected only by the use of the Bowles stethoscope attachment This murmur is transmitted in the direction of the regurgitant stream of blood and may be heard as far down as the cardiac apex The aortic regurgitant murmur is audible in early diastole a fact that at once serves to differentiate it from the late diastolic murmur of mitral stenosis In addition the diastolic murmur of aortic regurgitation is a high pitched blowing murmur while the diastolic murmur of mitral stenosis is low pitched and has a rumbling quality The mitral diastolic murmur is heard over a small area in the region of the apex while the aortic diastolic murmur has a much wider distribution

When the degree of rheumatic involvement becomes greater and the cusps of the aortic valve adhere a systolic murmur appears over this valve area which as the degree of stenosis increases becomes more harsh and more intense A systolic thrill is palpable over the aortic area at this stage and the aortic second sound is diminished or absent A plateau type of *pulse and a low pulse pressure can usually be demonstrated*

In any rheumatic case the physical signs of aortic or mitral valvular disease depend on the relative degrees of regurgitation or stenosis present If regurgitation is the main lesion at the aortic area the diastolic murmur is long and loud and the peripheral vascular signs striking while if stenosis predominates the systolic murmur over the aortic area will be the main element and the diastolic murmur although heard in the same area will be shorter and less intense When aortic regurgitation is marked there are characteristic alterations in the cardiac size and shape (see Fig

23) Often in patients with aortic insufficiency the degree of left ventricular hypertrophy is extreme

HEALED VALVULAR LESIONS at the mitral and aortic areas are the usual sequelae of rheumatic infection less often involvement of the tricuspid and pulmonary valves occurs Valvular lesions lead to cardiac hypertrophy and in the course of time are followed by heart failure A less frequent manifestation of rheumatic infection that may occur later in life is calcareous aortic stenosis Described first by Monckeberg in 1904 the etiology of this lesion has since formed the topic of much speculation Many clinicians consider it a manifestation of atherosclerosis others claim that it arises as a result of healing of a subacute bacterial endocarditis The majority of observers now consider it as a late manifestation of rheumatic heart disease [413]

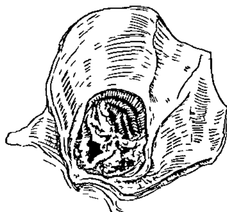


FIG 56 Rheumatic endocarditis The calcific type of aortic stenosis (viewed from above)

IN CALCAREOUS AORTIC STENOSIS fusion of all the cusps is usually seen (Fig 56) The reduced blood supply to this area favors the deposition of calcium and the degree of obstruction becomes extreme Many times these calcium deposits in the valve can be visualized by roentgenologic methods (see Fig 26) Calcareous aortic stenosis is much more frequently seen in males than in females and is accompanied by extreme cardiac hypertrophy It occurs at any age Angina may be present and this complication makes sudden death a possibility

SPECIAL METHODS OF EXAMINATION are valuable aids in the diagnosis of rheumatic infection Aside from the electrocardiographic examination the roentgen ray study (page 37) may be depended upon to reveal characteristic alterations in size and shape of the heart in the presence of all types of rheumatic disease The sedimentation rate is a valuable index of activity (page 57) while the blood count will reveal anemia and leukocytosis The blood culture shows no growth The urinary findings are influenced by the presence of active infection and congestive cardiac failure

## PROGNOSIS

The prognosis of rheumatic heart disease is difficult if not impossible to state when the patient is first examined Caution however must be used in giving too grave an outlook, especially in children in the presence of an active process (page 167) When the infection subsides and the heart balance is in some degree restored a continued although restricted existence, may be possible for many years Conduction defects disappear heart size diminishes even murmurs may fade from the picture along with the *active rheumatic state*[31] *Exceptional cases may recover to such an extent* that on future examination all evidence of the existence of so severe a carditis will be lacking

**Individual Factors** I do not believe that we can predict the outcome of acute rheumatic carditis in any patient by the course that the disease has previously pursued in brother sister or parent While heredity has some bearing on the patient s disease the progress and the ultimate degree of cardiac damage are individual factors and subject to wide variations It can be safely stated however that the earlier the onset the worse the prognosis and the greater the likelihood of cardiac involvement The disease has a tendency to pursue a more fatal course in females than in males It is important to determine and record the number of attacks in the history As a rule the greater the number of attacks the more likelihood there is of a resultant cardiac damage whereas if there is a definite history obtained of a number of rheumatic episodes and the heart shows slight damage it is unlikely that future recurrences will be *any more* severe As the patient grows *older and passes puberty the* physician is less fearful of the cardiac sequelae of the recurring attacks

The discovery of rheumatic nodules (Fig 54) aside from the value in clinching the diagnosis likewise aids in prognosis As a rule the patients showing typical nodules may be expected to have a stormy time and acquire early and usually serious cardiac damage A blond child under 10 who shows fever and nodules will usually cause many an anxious moment before signs of infection become quiescent

**The environment** has a decided influence on the progress of the disease[36 369] Poor housing conditions dampness and all the aspects of poverty that may be encountered contribute to persistence of the infection, while warmer climates sunshine, and good food have a favorable influence on the course of the disease and consequently are factors that support a more favorable prognosis

**Occupation** plays a decided role in prognosis If strenuous work is carried on by young men and women whose education has been frequently interrupted by episodes of acute rheumatic infection it leads to a greater degree of cardiac disability Those who are fitted for lighter and higher salaried positions survive longer, other things being equal

**Pregnancy** may add to the gravity of the prognosis in some cases (page 452), but it is surprising how well many patients with advanced lesions progress through one or even two pregnancies without adding to the cardiac embarrassment or inducing recurrence of the rheumatic process (Chapter 15) There is an unpredictable (and fortunately rare) danger of invasion of organisms that may attack the already damaged heart valves

**The occurrence of subacute bacterial endocarditis** naturally alters the prognosis at once In this event, instead of remaining a mild case of healed rheumatic infection with a good prognosis the patient becomes a hopeless case This is one of the major tragedies in the course of rheumatic heart disease

**Congestive Heart Failure** If the patient survives the acute attack of rheumatic fever *and is fortunate enough to avoid the complication of* subacute bacterial endocarditis the possibility of congestive heart failure in middle life lies ahead Slight lesions in patients who are carefully watched may be compatible with a long life Willius has shown that the average age at death of the patient with mitral disease is 30 years 32 years when both aortic and mitral valves are involved and 43 years when the aortic valve alone is affected [411]

**Thrombus Formation** In patients with advanced mitral stenosis the late course is very apt to be complicated by auricular enlargement and auricular fibrillation This combination paves the way for another danger for under these circumstances slowing of the blood current in the atrium favors thrombus formation Particles of the clots then become dislodged and form emboli

**Hemoptysis** Increase in the pulmonary pressure that follows advancing stenosis may cause capillary rupture and hemoptysis mav appear This symptom in later life again suggests the diagnosis of tuberculosis particularly if the patient shows fever and pallor and has a history of loss of weight However tuberculosis is very unusual in patients with mitral stenosis

## TREATMENT

While it is true that we are still groping in the dark for the cause of rheumatic infection careful management can accomplish much Except for the almost specific value of salicylate therapy in joint involvement we have no potent drug or serum to use in our fight which in most cases results in a long siege However gratifying results are many times possible if we adopt and follow a definite plan of therapy

The first essential to success is to obtain the full co-operation of the patient and his family This is accomplished by acquainting them with the nature of the disease and the basic principles of the method that will be used in combating it The more the patient knows about the type and extent of his cardiac disability the better equipped will he be for the future When the disease remains smoldering after the mildest and most

innocent onset the danger is usually the greatest for many times the patient's consent to the necessary limitations is apt to be obtained with difficulty

## Rest

Although there is a wide variation in the extent of the involvement and consequently in the symptoms presented by each patient the basic rules for management are the same for all The most successful treatment of rheumatic infection pays close attention to the cardiac condition Consequently when a diagnosis of a generalized rheumatic infection is established a rule of treatment should be to take it for granted that an acute myocarditis is present Exertion should therefore be totally restricted in all cases and the patient kept in bed until the signs of activity have faded

**When do we allow an increase in the activity?** This decision is not easy for there is no absolute guide that may be used in all cases The leukocyte count is not trustworthy in every instance The temperature may likewise be misleading since it is possible for activity to be present in many children who will show no temperature elevation The pulse rate while many times a most reliable guide is by no means an infallible one A drop in the pulse rate is a good omen in conjunction with the other signs but per se it may be misleading for bed rest in some patients may produce a satisfactory drop in the pulse rate in spite of a persisting and progressing infection

**The sedimentation rate** I believe is a valuable guide in determining the status of the disease (page 57) It is increased during the active phases and returns slowly to normal when infection subsides However the sedimentation rate is not a specific test for rheumatic infection since all inflammatory processes with or without fever influence it It is wise always to consider the sedimentation rate in the light of the other findings and never to depend upon a single determination as a guide to future treatment Comparative readings should always be made If these remain consistently high active rheumatic infection is present Occasionally the sedimentation rate will fall to normal in the presence of congestive failure, in this instance the fall may be regarded as a bad sign

Body Weight A record of the body weight should always be kept during the period of bed rest since a gain in weight occurs in convalescence, and when accompanied by other favorable signs it permits a cautious increase in activity As a rule the period of bed rest prescribed in each case will depend upon all the clinical evidence The minimum is usually two months, although much longer periods become necessary in severe cases

## Heart Hospital

Bed rest is most satisfactory in a special hospital or convalescent home although it may be possible in some selected instances to accomplish it in the patient's own home Environmental conditions in each case should guide the physician in making this decision




FIG 57 A The Children Heart Hospital B A school session Childrens Heart Hospital

Stroud and McMillan[36] have called attention to the need in this country of increased facilities for prolonged convalescent care of children with active and latent rheumatic carditis More specially equipped hospitals are needed, for they can carry on this work with a higner degree of efficiency than the ordinary hospital Each patient requires proper grading of his exercise and the supervision of workers who are skilled in the detection of signs of early activity But most important of all heart hospitals are equipped to carry on the long siege against rheumatic infection and do not neglect the scholastic education of their patients during the many months of bed rest (Fig 57) Education is the great need of the young cardiac patient because adequate training may enable him to obtain a sedentary occupation at a later date

Children are admitted to heart hospitals for long periods usually from 12 to 18 months and only those cases are accepted that may be expected to derive benefit from the course of treatment The requirements for admission to the Children s Heart Hospital in Philadelphia are as follows [360]

1 *Age limit Boys 3 to 1[illegible] years girls 3 to 13 years*
2 Children shall have either possibl[illegible] or pot[illegible]ntial heart disease
3 No patients who have had congestive cardiac failure or who have a hopeless prognosis shall be admitted
4 Before admission each child shall spend at least two weeks in a hospital
5 As far as possible all foci of infection should be removed
6 Parents shall agree that children will remain in the hospital from three to six months or longer, at the physician s discretion

TABLE IV

DAILY ROUTINE IN CHILDREN S HEART HOSPITAL (Stroud and McMillan)

| | | |
|---|---|---|
| Temperatures | 7 to 7 30 a m | |
| Breakfast | 7 30 a m | |
| *Older children attend school from* | 9 to 11 30 a m | |
| Younger children rest from | 9 30 to 11 30 a m | |
| Younger children attend school from | 11.30 *to* 12 30 p m | |
| Older children rest from | 11 30 to 12 30 p m | |
| Dinner | 12 30 p m | radio |
| Temperatures | 1 to 1 30 p m | |
| Younger children attend school from | 1 30 to 3 p m | |
| Older children play until 2 30 and rest from | 2 30 to 4 p m | |
| *Younger children rest from* | 3 to 4 p m | |
| Play hour | 4 *to* 5 15 p m | |
| Temperatures | 5 15 p m | |
| Supper | 5.30 p m. | *radio* |
| Bedtime | 6 15 p m | radio |

*Trans Sec D s of Children of Amer Med Asso 1927 Reprinted by permission of Amer Med Asso

Table IV gives an idea of the average schedule of the patients in the Children s Heart Hospital in Philadelphia Reviewing the first 225 cases subjected to this special environment and care Stroud and McMillan reported marked improvement in 108 children These patients on discharge were able to carry out practically the same daily routine as healthy children of the same age and social status

During the prolonged convalescent period that follows an attack of

rheumatic infection regular visits to the physician s office should be made The patient should be told that these visits are not for the purpose of obtaining medicine, but for the detection of any clue that might suggest a recurrence of the infection When the physical status is determined at each follow up examination suitable adjustments in the exercise allowance may be made This prescription is based on the extent of the lesion and the weight but is mostly governed by the symptoms if any produced by the previous exercise allowance In the case of children a contact should be established with the school authorities in order that co-operation may be obtained in carrying out the planned program

Some patients visit their physician every month others every two three or even six months as the circumstances demand It can be truthfully stated that advanced cardiac disease develops more often in those who refuse to co-operate with the physician or clinic in the matter of these routine follow up examinations However it seems that it will always remain a problem to convince patients and their parents of the necessity of regular visits to the doctor when they feel fine particularly when no special therapy is carried out at the time of the visit and no prescription for medicine is forthcoming Many times in cases of this type some form of physiotherapy or even a placebo may prove valuable in management After all anything that ultimately proves of advantage to the patient may be viewed as good treatment

## Management of Arthritis

Although I cannot prove my point by an array of statistics I believe that the joint manifestations of rheumatic infection are less often seen today than they were 20 years ago A possible explanation lies in the freer use of proprietary preparations earlier in all fevers by the modern American family

**The salicylates** have a specific action on the joint manifestations of rheumatic fever When they fail the reason is either insufficient dosage or a mistaken diagnosis Sodium salicylate in doses of 4 0 to 7 0 Gm (60 to 100 grains) daily in small children and higher in older children and adults usually eliminates all joint symptoms within 24 hours The fever likewise decreases as the joint signs disappear (see Fig 59) Salicylates should always be administered with an alkali in the form of an equal amount of bicarbonate of soda The error frequently is made in giving too small rather than too large doses of sodium salicylate If gastric irritability occurs with doses which are inadequate to control the joint symptoms the salicylate can readily be given by bowel A dose of 8 0 Gm (120 grains) mixed in eight ounces of thin starch paste may be given twice daily Only rarely is it necessary to resort to the intravenous use of salicylate but when necessary a 10 cc ampule of a 20 per cent solution can be given two or three times a day Prompt relief of pain follows this method and if the injections are given slowly reactions are few

Administration of salicylates in very large doses will produce in some

patients a toxic state due to acidosis, and it is most important to recognize this if it occurs Vomiting is a common symptom at the onset and may be followed by increased respiratory rate fever, restlessness and coma Salicylism may be confused with diabetic acidosis, but the differentiation is possible by blood sugar determination Tinnitus deafness twitching convulsions and delirium are symptoms more characteristic of salicylate poisoning than diabetes Toxic signs following excess salicylate administration are accompanied by a lowering of the carbon-dioxide level of the blood The symptoms are relieved by alkalis

The joints involved in acute rheumatic fever should be wrapped in cotton and protected from the weight of the bed clothes A 20 per cent methyl salicylate ointment may be used if preferred Since careful nursing care is most essential the acute cases should be sent to the hospital whenever possible

## Management of Chorea

When the rheumatic infection invades the brain and choreiform movements develop the patient should be moved to a peaceful quiet environment Again efficient nursing care is essential If the movements persist sedatives should be used freely Either elixir of phenobarbital 4 0 cc (1 fl dram) sodium bromide 0 6 to 1 0 Gm (10 to 15 grains) or chlorotone 0 3 Gm (5 grains) given after meals for a few days are helpful The salicylate medication should be continued Although the drug has no specific effect on either the nervous system or cardiac involvement it is well to continue its use if the rheumatic invasion is active in localities other than the joints and is attended by pain

**Fever Induction** The most recent and perhaps the most useful form of therapy for rapid relief of the symptoms of chorea is fever induction by means of the Kettering apparatus [307] While it is possible to produce fever by intravenous injections of typhoid bacilli it is best to use the induction method Lately other forms of rheumatic infection have been treated by fever induction and claims made that it shortens the duration of the attacks (page 523)

## Other Forms of Therapy

**Tonsillectomy** Since the belief that the tonsils are the portals of entry of the rheumatic infection is prevalent no time is usually lost in removing them as soon as rheumatic activity is suspected Often this is a grave risk for severe recurrences after tonsil operations are not at all uncommon **Tonsillectomy should be carried out only when the infection has been found to be quiescent It is never an emergency**

While considerable difference of opinion prevails concerning the ultimate value of this procedure it is certainly wise to plan a tonsillectomy in rheumatic patients who show evidence of tonsillar hypertrophy infection or secondary involvement of the cervical glands Some protection against the temporary blood stream invasion that may follow is offered by the

administration of sulfanilamide in the proper dosage before and for a short time following the operation (page 198). While sulfanilamide may be of value in preventing a dangerous bacteremia following tonsillectomy, it does not affect the course of established rheumatic infection.[61, 60, 370]

**Dietary measures** should be directed toward keeping up the body weight. A high caloric high vitamin diet is valuable. This may be fortified by the addition of 50 mg. of crystalline ascorbic acid (vitamin C) twice daily and 4.0 to 5.0 Gm. of brewer's yeast (vitamin B) daily in the form of tablets (Chapter 21).

**Sera and Vaccines.** Attempts at a more specific type of therapy have led to the administration of various sera and vaccines. The results reported show no uniformity and are all open to question. It must be remembered that we do not know the exact nature of the rheumatic infection and until we do, such favorable results that follow the injection of the various preparations made up from the streptococcus must be regarded as non specific. I have seen the indiscriminate use of vaccines many times light up a previously inactive rheumatic infection. Although I do not deny that the introduction of foreign protein will aid the mechanism of defense in some cases, I do not feel justified in attempting it, particularly when the patient is progressing slowly with the aid of his natural forces. "The infection that sleepeth harmeth nobody."

**Prevention of recurring upper respiratory tract infection** in our rheumatic cases* would be a most efficient means of lessening the number of attacks of rheumatic fever. Coburn[60] and others have transported rheumatic children to tropical and subtropical climates and have demonstrated that they are free of upper respiratory infection in these warmer latitudes and that all the rheumatic manifestations subside, to return again when they are re exposed to the climatic conditions of the northern seaboard states.

**Roentgen ray treatments** over the precordium have been advocated by some workers in the hope of limiting infection and minimizing cardiac damage. As far as I can determine, these exposures have no effect whatsoever on the heart and appear to be ineffective and represent purely local thrusts at a generalized disease. Levy and Golden have recommended roentgen ray therapy for various forms of rheumatic infection which show a low grade of activity. The changes recorded in the electrocardiogram, the clinical improvement and the relief of pain experienced by some cases suggested to these observers that such exposures have had a beneficial effect. They have reported a series of 48 cases seen during the past 11½ years. No harmful effects of irradiation were noted. The manner in which improvement is accomplished is unknown.

**Valvulotomy.** The surgical procedure of valvulotomy in mitral stenosis, aside from the difficulty in the technic and the risk involved, offers little even if successful, for the fibrous tissue in the valve may soon re establish

* Utopia in Philadelphia

the stenosis Where marked cardiac hypertrophy is present, rib resection has been occasionally successful

## PREVENTIVE MEASURES

Early recognition of all the manifestations of the rheumatic state from growing pains to frank articular involvement and prompt treatment may aid in preventing advanced cardiac change Where carditis is the only sign of the presence of the disease, frequent physical examinations of all school *children make possible the early recognition of rheumatic infection* Suspicion of its presence should be entertained in all children who show pallor anemia loss of weight and who complain of weakness or frequent unexplained nosebleeds By the discovery of early cardiac involvement we may in some measure prevent advanced hopeless lesions

As far as the actual prevention of the disease itself is concerned further investigations are needed by both clinician and laboratory worker As Coombs[7] has stated

> Life is short—but art is long and it is useless to attempt the annihilation of such a disease as this by an 'intensive campaign — To the conquest of disease there can be no short cuts It is a painful hand to hand struggle in which everyone must be mobilized and in no part of the battle front is there better opportunity for successful co operation between all sections of the profession—general practitioner consultant and administration—than in that on which we are faced by rheumatic heart disease

## ILLUSTRATIVE CASES

### Suspected Rheumatic Heart Disease—The Evaluation of the Systolic Murmur When It Represents the Only Abnormal Finding

**Case 9** P F *male aged 10 years was sent to the Cardiac Clinic of the Memorial* Hospital on May 2 1936 by a school physician Complaints were nervousness and slight weight loss

History The birth had been normal There was no history of rheumatic infection He had a tonsillectomy at the age of five There were no subjective symptoms referable to the cardiovascular system

Physical Examination Well developed lad Throat clean Entire examination normal except for the presence of a soft, systolic apical murmur poorly transmitted into the axilla The apex beat was in the fifth intercostal space well inside the mid clavicular line The heart sounds were normal B P 110/80

*Laboratory Data Wassermann reaction negative* Blood count normal Sedimentation rate 5 mm in one hour (Fig 58C) A roentgen study (Fig 58A) showed no cardiac enlargement The electrocardiogram (Fig 58B) was normal

Clinical Diagnosis Class E Signs referable to the heart but the diagnosis of heart disease cannot be proved Murmur functional in type Activity unrestricted

Discussion Well established lesions at the mitral valve accompanied by cardiac enlargement usually offer no difficulty in diagnosis However a systolic murmur heard at the apex in otherwise healthy children continues

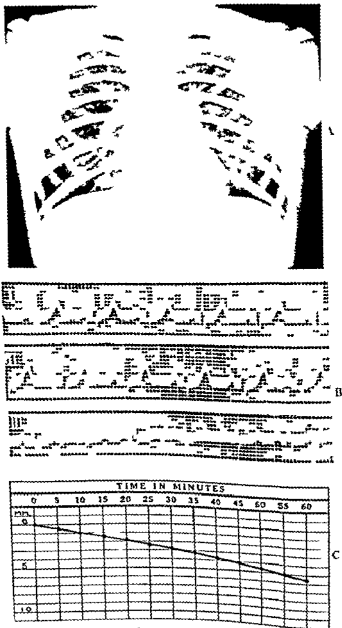



FIG 58 A The roentgenogram shows no cardiac enlargement
B The electrocardiogram is within normal limits The notching and low voltage of QRS3 not infrequently occur in the tracings of normal patients
C Sedimentation chart The red blood cells show a fall of 6 mm in one hour

to be a stumbling block in cardiac diagnosis Although I admit that in some cases the correct interpretation at the time the child is first seen is difficult or impossible the evaluation of the importance of the finding in the majority of cases presents very little difficulty if certain fundamental facts are kept in mind

In the first place many healthy children may show a transient soft apical systolic murmur following excitement or exercise when the speed of the circulation is increased It may likewise accompany fever or anemia The murmur in this region may be heard only during a certain phase of respiration or it may appear when the patient is in recumbency, disappearing in the erect position The terms 'functional' "hemic' and cardiorespiratory ' are used in describing the systolic murmurs accompanying these conditions Although these are acceptable terms care should be used in describing the intensity pitch quality and duration of the murmurs heard (page 19) If this is done in all cases, the data obtained aids in the correct evaluation of the finding For example functional murmurs are more apt to be faint or moderate in intensity, while loud murmurs are nearly always associated with organic heart disease Harmless murmurs are more apt to be short and blowing while those of long duration particularly if they are harsh rumbling or crescendo, generally accompany disease of the valvular structures

This boy had a faint blowing systolic murmur over the mitral area Its duration was short and it increased to moderate intensity in the recumbent position Examination showed the absence of cardiac enlargement So far the criteria for a functional murmur have been fulfilled However the findings must be viewed in the light of the patient s past history Did he have rheumatic fever or chorea? All we can elicit is a history of nervousness It is unlikely that this symptom is related to chorea, since the blood count sedimentation rate temperature and weight furnish no supporting clues

If the patient had given us a clear cut history of rheumatic fever the evaluation of the murmur would have been more difficult In these cases, if no cardiac enlargement accompanies the systolic murmur and in the presence of negative laboratory studies a definite answer cannot be given at once Re examination should be made two or three times a year Meantime since we are aware of the frequency of valvular disease following rheumatic fever full activity should not be allowed Certainly competitive sports should be eliminated until the child is older If as time goes by and puberty is passed the findings remain constant we can be certain that the heart has escaped and full activity may be permitted On the other hand if the murmur becomes louder and longer and cardiac enlargement appears accompanied by an increased pulmonic second sound a mitral regurgitation is probably present

Sometimes the systolic murmur in the mitral area disappears This is possible following the correction of severe anemia (page 424) or hyperthyroidism (page 356) A rapid heart rate following exercise may be accom

panied by a systolic murmur that disappears following rest In these instances the increased velocity of the blood accounts for the producti n of the murmur

## Rheumatic Heart Disease—Acute Carditis Following Typical Joint Involvement—Mild Course

**Case 10** Mrs C Z a housewife of 7 was well unt l two days before a l mission to the Woman s College Hosp tal on D cember 7 1938 She first noticed sore throat which was followed a week later by high fever s eating and pain and swell ng in the l ft knee There was no history of previous similar attacks

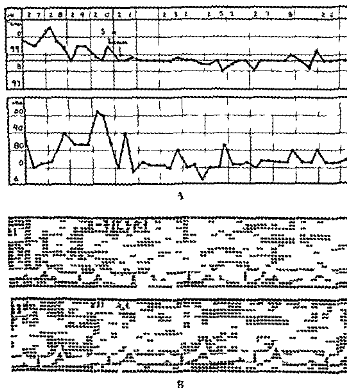


Fig 59 A Temp rature pulse record

B The el ctrocard ogram In the first record (lead ) taken on 1 /14 38 note prolongat on of the P R In rvals o 0 3 econd In the second record (sa ne lead) taken on 1 10/39 the P R Intervals are nor nal

Physical Examination B P 110 80 T 00 F Pulse 86 Re p rations 20 Well nourished adult fem l not acutely ill T ns ls red and enlarged The l ft knee was s ollen an l tend r v th re tri ted motion The heart was normal in siz The ap x beat was palpable in the fifth nterspa e s ll in de the midclavi ular line A soft systol c murmur was hear l in the mitral area. The rhythm was regular

Laboratory Data W B C 13 000 R B C 4 500 000 He noglob n 84 per ent (Sahl ) The electrocard gram show d prolongation of the P R intervals to 0 34 second (F g 59B)

CLINICAL DIAGNOSIS A Etiologic Rheumatic Active B Anatomic No cardiac enlargement Mitral regurgitation?? C Physiologic First stage heart block (Prolonged P R intervals) D Functional Classification Class I Therapeutic Classification Class E

Discussion The onset here is quite typical An attack of tonsillitis was followed by pain and swelling in the left knee It would be hard to ignore such evidence The large infected tonsils that were seen in this patient withstood many attacks but the rheumatic invasion finally took place In younger patients who have had one or more attacks of rheumatic fever, upper respiratory infections of any type are capable of producing fresh invasions The common head cold must be viewed as a serious complication in a rheumatic subject Each cold threatens to increase the amount of cardiac damage should it succeed in lighting up a latent infection Consequently the rheumatic patient should always go to bed for a few days when the first signs of a head cold appear Unnecessary contacts with individuals who have colds should be avoided as much as possible The rheumatic subject should also be carefully examined for signs of activity when the symptoms of respiratory invasion have subsided

Bed rest and salicylates were prescribed on admission in this case The specific action of salicylates on the joint symptoms is readily seen in the temperature record (Fig 59A) Four days after admission definite evidence of an acute inflammation of the heart appeared in the electrocardiogram (Fig 59B) This finding was valuable in planning the subsequent management Since the patient felt so much improved after the salicylate therapy, it was difficult to persuade her to remain in bed She was a farmer s wife always used to hard work and had three children waiting at home When the situation was explained the patient consented to remain in the hospital for a longer period of supervised bed rest Salicylates were dropped at the end of the second week and since there was no recurrence of fever or joint pain they were not used again The salicylates could have had no influence whatsoever on the course of the carditis

During the next eight weeks of her stay in the hospital no other drugs were used The patient was placed on a high caloric diet and cevitamic acid (vitamin C) was given in 20 mg doses t i d The tonsils although large and infected were allowed to remain They will not be removed until full proof is at hand that the rheumatic infection is quiescent

When the patient was discharged from the hospital to continue her convalescence at home, the following program was written out and given to her

First week Sit up in chair beside the bed one hour in the afternoon
Second week Sit up in chair for two hours every afternoon
Third week Sit up in chair one hour in the morning and two hours in the afternoon May walk to the bathroom on the same floor
Fourth week Sit up in chair for two hours in the morning and two hours in the afternoon Walk to the bathroom on the same floor
Fifth week Same
Sixth week Up from 10 A M to 5 P M Do not go downstairs

Seventh week Up from 10 A M to 5 P M May go downstairs at noon and remain there until after dinner
Eighth to tenth week Same
Eleventh week Downstairs for meals One half hour walk out-of-doors in the afternoon
Eleventh to fifteenth week Same but increase walk to one hour by the end of the 15th week
Notes Keep a temperature chart for the first eight weeks Full diet Continue tablets of cevitamic acid (60 mg daily)

Viewing the soft systolic murmur that was heard over the mitral area of this patient on admission in the light of the typical findings we cannot say that it is functional even in the absence of cardiac enlargement During the early days of the infection when a high fever was present the murmur may have been functional in the sense that it was produced in a toxic myocardium by relaxation of the mitral ring Actual inflammatory changes may have already developed in the valve distorting its leaflets and directly interfering with its function When these murmurs persist during the months following convalescence it is reasonable to suppose that they are caused by disease of the mitral valve itself Mitral regurgitation should then be the tentative diagnosis especially if cardiac enlargement can be demonstrated It is true that the diagnosis of mitral regurgitation is very rarely upheld at necropsy However it is equally true that patients do not succumb during this stage of the disease Survival permits contraction and healing of the valve leaflets to take place and mitral stenosis develops Consequently if signs of stenosis are discovered in a patient suffering from acute rheumatic fever, previous attacks should be suspected

## Rheumatic Heart Disease with Aortic Regurgitation No Signs of Active Infection and Slight Cardiac Enlargement

**Case 11** F N a 16 year old school boy was sent to the cardiac clinic at the Woman s College Hospital in January 1931 A heart murmur had been discovered by the school physician

History Negative for rheumatism All previous physical examinations were negative No symptoms were present referable to the cardiovascular system The patient had always been active in school athletics and the exercise tolerance was good

Physical Examination B P 130/60 Apex beat in the midclavicular line 8 5 cm to the left of the midsternal line in the fifth interspace The pulse was 80 and of the Corrigan type and the rhythm was regular There was a blowing diastolic murmur along the left sternal border

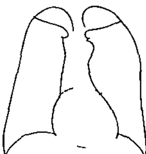
Laboratory Data Wassermann negative Blood count normal One urinalysis negative Sedimentation rate normal The orthodiagram (Fig 60A) showed slight cardiac enlargement The cardiothoracic ratio was 0 46 the transverse cardiac diameter was 12 9 cm (predicted 11 8 cm) and the cardiac area was 129 sq cm (predicted 115 sq cm) The electrocardiogram (Fig 60B) showed slight flattening of $T_1$ There was no axis deviation

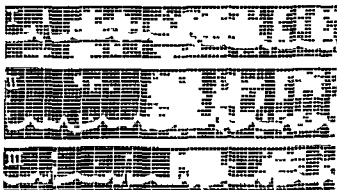
Clinical Diagnosis A Etiologic Rheumatic Inactive B Anatomic Slight cardiac enlargement Aortic regurgitation C Physiologic Normal sinus rhythm D Functional Classification Class 1 Therapeutic Classification Class B

Discussion Watching this lad over the course of the nine years that he has been visiting our clinic has been most instructive When he first came to us during the winter of 1931 he presented the typical picture of aortic

regurgitation No signs of mitral disease were elicited and to confuse the issue further he gave no history of rheumatic infection

The initial study showed the absence of cardiac enlargement, a flat $T_1$ in the electrocardiogram a negative Wassermann and a very good exercise tolerance Since the majority of patients who have organic heart disease at this age belong to the rheumatic group he was tentatively placed in this category and tests were made to rule out the presence of activity Again blood studies including a leukocyte count and sedimentation rate, were normal He was gaining weight and aside from his cardiac lesion appeared to be in excellent physical condition He was advised to discontinue basket ball but no other restrictions were imposed





A B

FIG 60 A The orthodiagram shows slight cardiac enlargement Note prominent aortic knob
B The electrocardiogram There is slight flattening of $T_1$ The P waves are widened in lead There is no axis deviation

Although our suggestions were carried out by the school authorities, the patient admitted at each visit that he was participating in competitive sports of all kinds There was no dyspnea As the years went by we felt less concern when we noted that the heart size and other features of the examination remained exactly the same as initially recorded

For eight years this boy has enjoyed unrestricted activity and has taken part in competitive sports against advice However our protests in recent years have been milder, when we observed the absence of any demonstrable ill effect The exercise that we prohibited appears to have added to his mental and physical well being At the age of 24 his chief dangers appear to be the chance development of subacute bacterial endocarditis on the previously damaged heart valve and the recurrence of the rheumatic infec tion As he grows older the latter danger becomes much less although unfortunately the former possibility remains

During the time this patient has been under our care no routine medication of any kind has been prescribed A tonsillectomy was performed

during the first summer, and he has had a routine dental examination every six months

RHEUMATIC HEART DISEASE—ACTIVE INFECTION—DEATH FROM CONGESTIVE FAILURE AT UNUSUALLY EARLY AGE—AUTOPSY

**Case 12** E W a male infant of 3½ years was admitted to the Philadelphia General Hospital on 6/7/37 and died on 6/11/37 Chief complaints on admission were fever and frequent nose bleeds

HISTORY Bronchopneumonia at 2½ months whooping cough at one year and measles at the age of two Two months prior to admission the patient began to have fever at night and there was a steady weight loss Frequent severe nose bleeds followed and continued until the day of admission

PHYSICAL EXAMINATION showed an acutely ill child pale slightly cyanotic and poorly nourished T 101 P 1 0 R 35 Pale conjunctivae teeth carious The tonsils were large and cryptic The lungs were clear The heart was enlarged to the right and left The apex was well beyond the midclavicular line where a diastolic thrill was palpable A blowing systolic murmur and a rumbling diastolic murmur were heard in the mitral area A to and fro murmur and a systolic thrill were present over the aortic area The liver was palpable four fingers below the costal margin The fingers and toes were short and stubby Rheumatic nodules were palpable on the right knee and the left ankle

LABORATORY DATA Urine negative Blood hemoglobin 49 per cent (Sahli) R B C 700 000 W B C 9 000 Sed mentation rate 8 mm in one hour The roentgenogram showed cardiac enlargement in all diameters

CLINICAL DIAGNOSIS A Etiologic Rheumatic Active B Anatomic Cardiac enlargement Aortic stenosis and insufficiency Mitral stenosis and insufficiency C Physiologic Normal sinus rhythm Congestive failure D Functional Classification Class 4 Therapeutic Classification Class E

**Discussion** Evidence of an active rheumatic infection was present on the first examination In addition to the signs of an unusual degree of cardiac involvement in one so young the cyanosis dyspnea and large liver pointed to congestive failure

In the presence of acute carditis the mechanical strain of the valvular lesions has a much less important place Congestive failure when it occurs in children is usually in itself evidence of activity and if carefully searched for the signs will be brought to light In this child rheumatic nodule were palpable on admission

In cases where the overwhelming infection precipitates cardiac failure digitalis is of doubtful value Nevertheless it should always be given (page 84)

Since cyanosis was marked the child was placed in an oxygen tent which seemed to have little influence on the course of the disease The respiratory rate mounted and the congestive manifestations increased One half cc of mercupurin in 10 cc of saline was given intravenously but had little effect Death occurred on the fourth hospital day

AUTOPSY The heart (Fig 61 A and B) weighed 150 Gm The epicardium was gray and glistening The myocardium was moderately flabby and contained numerous delicate gray streaks and pin point bright pink areas especially near the endocardial surface The auricular endocardial surface was thick and opaque The free edges of the mitral valve were thickened and scarred The mitral chordae were thickened shortened and adherent The aortic orifice was narrowed just admitting a small probe The aortic

leaflets were thickened rigid and firmly glued together The valves on the right side of the heart appeared normal The foramen ovale was closed The coronary vessels were normal




Fig 61 Rheumatic heart disease There is a characteristic shortening and fusion of the aortic leaflets resulting in stenosis and insufficiency (Autopsy No 33 574 Philadelphia General Hospital )

## Rheumatic Heart Disease with Mitral Stenosis and Congestive Failure—Influence of Multiple Pulmonary Emboli on Course and Prognosis

**Case 13** Mrs A H a white housewife of 5 was admitted to the Philadelphia General Hospital on /13/34 complaining of cough shortness of breath and swelling of the legs

History Increasing dyspnea during the past year A week before admission edema of the legs developed and was followed by chest pain cough and hemoptysis Her mother had Tb and heart trouble No history of rheumatic infection The patient considered herself in good health until a year before admission

Physical Examination P 120 (irregular) B P 145/90 Jaundice was present The neck veins were distended There were rales at both lung bases There was edema of the legs to the hips

The heart was enlarged L B 13 0 cm to the left of the midsternal line There was a short diastolic murmur over the region of the apex beat The liver edge was distinctly palpable 7 cm below the costal margin in spite of distention and shifting dulness in the abdomen (Fig 6 A)

The electrocardiogram showed auricular fibrillation with a rapid ventricular rat (Fig 6 B)

Clinical Diagnosis A Etiologic Rheumatic Inactive B Anatomic Cardiac hypertrophy Mitral stenosis and insufficiency C Physiologic Auricular fibrillation Congestive cardiac failure D Functional Classification Class 4 Therapeutic Classification Class E

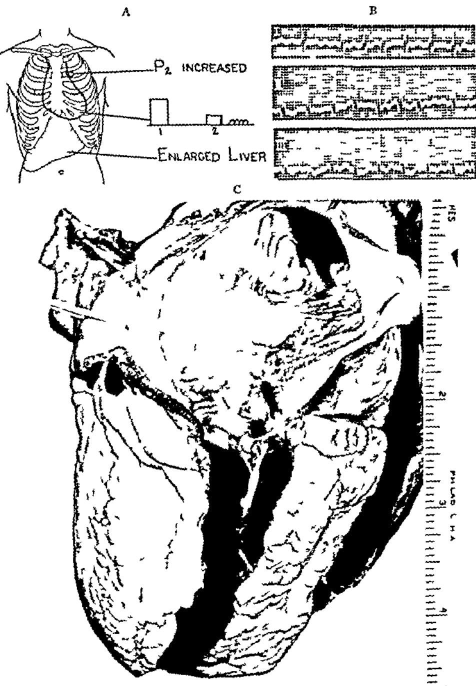



Fig 6 A Chart of physical findings B The electrocardiogram Auricular fibrillation is present with a rapid ventricular rate
C Rheumatic heart disease Mitral stenosis is present with marked dilatation of the left auricle Note that the size of the auricle is nearly equal to that of the ventricle (Autopsy No 27 081 Philadelphia General Hospital)

COURSE Down hill from time of entry The patient showed no response to digitalis and diuretics and died on the ninth hospital day

AUTOPSY (Fig 6 C) Rheumatic heart disease with mitral stenosis and cardiac hypertrophy The auricles were dilated There were multiple pulmonary infarcts Pulmonary atherosclerosis Congestive cardiac failure

**Discussion** The diagnosis of the type of heart disease present in this patient was not difficult even in the absence of a definite rheumatic history *Symptoms began a year before admission at the age of 51 showing that* advanced mitral disease may at times be present for many years and cause no disability Dyspnea was first noticed This increased gradually over the course of a year and finally a week before admission edema appeared and progressed so rapidly that she was forced to enter the hospital

Since this was the first spell of congestive failure in a patient who had rheumatic heart disease a form that is usually characterized by the ability to weather many episodes of decompensation we felt certain that circulatory *balance would be quickly restored following the use of digitalis in* proper dosage with suitable diuretics The combination of heart failure and auricular fibrillation with a high ventricular rate led us to adopt an attitude of optimism that future events proved was unjustified Although the history of pulmonary infarction was clear cut we failed to consider the unfavorable effect that this complication of advanced mitral disease has on the outcome in the presence of congestive failure

A proper evaluation of the symptom of hemoptysis during the course of *mitral disease is important if these errors in prognosis are to be avoided* Sudden episodes of chest pain dyspnea and hemoptysis do not always accompany a pulmonary infarction However dyspnea that becomes progressively worse followed by hemoptysis and the signs of congestive failure and shows no improvement when proper treatment is instituted should always suggest the presence of a pulmonary infarct

McGinn and White [17] in an analysis of the incidence of pulmonary infarction in 52 cases of mitral stenosis in 2500 consecutive necropsies *showed that this complication occurred in 61 per cent of 23 cases where* congestive failure appeared and in only seven per cent of the cases when congestive failure was absent In contrast to this group a study of 82 cases of hypertension showed 39 cases of congestive failure in 21 per cent of which there was pulmonary infarction

When symptoms suddenly become aggravated as in this case and are followed by collapse and increase in the signs of cardiac failure, pulmonary infarction should be suspected (Fig 63) Hemoptysis and chest pain may or may not be present If the patient survives a local pleural friction rub often appears and is followed by fever and leukocytosis A few days later jaundice may be noticed which is of the hemolytic variety and follows the extra burden placed on the already congested liver by the blood pigment from the pulmonary infarct In this patient an icterus index of 20 was obtained a few days after admission

The pulmonary infarction that so commonly complicates advanced

mitral disease accentuating the signs of congestive failure and rendering the patient so refractory to treatment does not always follow embolism Quite often conditions in the pulmonary circuit predispose to thrombosis There is usually present a sclerosis of the lung vessels and when a slowing of the blood current through them occurs during the early stages of heart failure spontaneous clotting is favored An infarct then develops its size

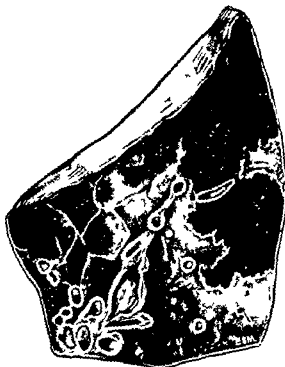


Fig 63 Hemorrhagic infarct of the lung

depending on the caliber of the vessel obstructed At times the discovery of dulness over these areas of infarction in a patient who shows fever and other signs of an active rheumatic process leads to a diagnosis of rheumatic pneumonia Again in cases where the onset is sudden and the area of infarction large the diagnosis of a lobar pneumonia may be made especially if chest pain a temperature elevation hemoptysis and a pleural friction rub appear

The course of rheumatic heart disease is often complicated by embolism after the onset of auricular fibrillation at which time considerable hypertrophy of the atrial musculature is generally present Under these circumstances the detachment of a part of a thrombus and its lodgment in the

lung is not unusual *Pulmonary embolism may also follow thrombosis in* one of the large pelvic or thigh veins although the exact site of origin may be unrecognizable clinically

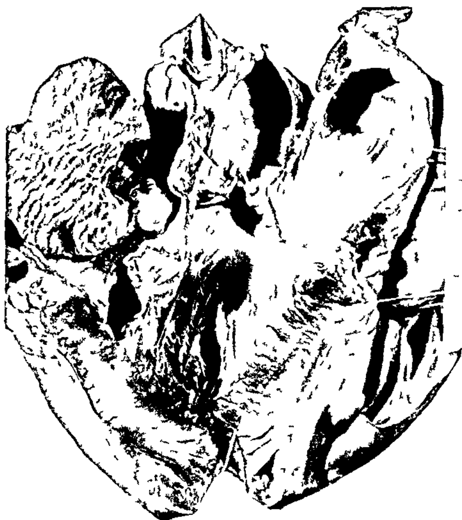


FIG 64 Rheumatic heart disease Note cardiac hypertrophy aortic and mitral stenosis The aortic valve (marked by arrow) is viewed from the sid Its leaflets are fused and thickened A large thrombus with a rippled surface almost completely fills the left auricle The mitral orifice (seen below the thrombus) is sclerosed and contracted (Autopsy No 30 167 Philadelphia General Hosp tal)

The auricular appendages are the common locations for thrombus formation In some cases we may be unable to prove the point of origin of the embolus if no clot is found at autopsy, while in others the whole auricle may be filled with thrombus (Fig 64) Occasionally following coronary

thrombosis mural thrombi may form in the left ventricle (see Fig 109) These particles may become detached and find their way into the systemic or cerebral circulation with serious consequences Ulcerative plaques in patients with advanced arteriosclerosis are often the sites of formation of thrombi that may eventually become dislodged Aneurysms or injured vessels likewise may be the starting points of emboli In chronic valvular disease it is rare for emboli to arise from the vegetations on the heart valves while the auricular source is quite common On the other hand in acute and subacute bacterial endocarditis fragments frequently become detached from the valves and since the mitral and aortic valves are involved most often the embolic signs appear in the systemic circulation

RHEUMATIC HEART DISEASE—MITRAL STENOSIS—EMBOLIC MANIFESTATIONS

**Case 14** M M a 30 year-old white clerk was first seen in July 1936 complaining of cough and shortness of breath He had been well until two days before when he developed a severe head cold This was followed by fever and cough and he noticed for the first time that his feet were swollen and that his pulse was rapid and irregular He gave a history of two attacks of chorea the first at the age of seven and the second at the age of 13

PHYSICAL EXAMINATION Temperature 100 F There was a totally irregular pulse of 120 and the respiratory rate was 3 The blood pressure was 1 0/80 Scattered ales were present in both lung bases There was pitting edema of both ankles The heart was slightly enlarged to the left The first sound was accentuated in the region of the apex and a mid diastolic murmur was heard in the same area P was accentuated

CLINICAL DIAGNOSIS A Etiologic Rheumatic (Chorea) Inactive ( ) B Anatomic Cardiac enlargement Mitral stenosis and regurgitation C Physiologic Auricular fibrillation Congestive cardiac failure D Functional Classification Class 4 Therapeutic Classification Class E

DISCUSSION The patient was placed at bed rest at home and complete digitalization was accomplished in three days (page 82) Codeine sulfate 0 03 Gm (½ grain) and ammonium chloride 1 0 Gm (15 grains) were given every four hours On the second day 1 cc of mercupurin was given intravenously These measures were sufficient to dispel all signs of congestive failure and to lower the pulse rate to 75 (see Fig 247B) On the fourth day the digitalis was decreased to 0 1 Gm (1½ grains) of the whole leaf daily At the beginning of the third week the patient was allowed to return to work on a restricted program

During the course of the next three years he was examined every three months The auricular fibrillation continued but no signs of congestive failure were discovered at any time His exercise tolerance was fair

In August 1939 following another upper respiratory infection the patient again developed cough but on this occasion there was hemoptysis The pulse rate rose to 130 and digitalis appeared to be ineffective in controlling the fibrillation Bed rest and mercurial diuretics however were finally successful in restoring the balance In five weeks the congestive failure disappeared and the dyspnea improved Digitalis 0 1 Gm (1½

grains) daily and ammonium chloride 1 0 Gm (15 grains) three times daily were continued

One month later, while at work he experienced a sudden pain in the left leg accompanied by numbness and coldness He was removed to the hospital at once At an emergency operation removal of an embolus from the left femoral artery at the site of origin of the profunda was successfully accomplished However the patient died suddenly the next day, following a cerebral embolism An autopsy was not obtainable

This patient presents the picture of chronic rheumatic heart disease with mitral stenosis The infection occurred early in childhood but no symptoms were present for over 17 years Death occurred three years after the onset of symptoms

The first attack of congestive failure appeared rather suddenly following an acute upper respiratory infection, which is not at all unusual Infection of this type is a much more common cause of a break in compensation than overwork although there is a widespread belief that the opposite is true There was no relighting of the rheumatic process inasmuch as compensation was quickly restored and the temperature returned to normal in a few days

Digitalis was begun when congestive failure first appeared and was continued in a maintenance dose to keep the ventricular rate between 70 and 75 until the patient s death three years later In his case the amount needed was 0 1 Gm (1½ grains) daily

Many cases of chronic rheumatic heart disease pursue a similar slow course over many years with occasional breaks in compensation that respond quickly to bed rest and intensive treatment Such a course is possible but is less often observed in cases of arteriosclerotic and hypertensive heart disease while it is quite unusual in cases of syphilitic heart disease

This patient s final illness was again ushered in by respiratory symptoms However this time he had hemoptysis and although there was nothing on physical examination to prove pulmonary infarction the history suggested this possibility Pulmonary infarction also accounted for the poor response to therapy on this occasion and changed the prognosis since we were prepared to expect recurrence of the accident in the same or other locations A month later an embolus from the dilated left auricle found its way into the left femoral artery Emergency surgical measures were successful but a day later cerebral embolism caused the patient s death

The patient whose heart is shown in Fig 64 was a white male of 33 who died following a clinical course quite similar to that of the patient just described The heart here is enormously enlarged with mitral aortic and tricuspid valve involvement the mitral and aortic valves showing an advanced stenosis The greatly dilated left auricle is completely filled by a large ball valve thrombus This complication of the rheumatic valvular disease was the direct cause of death that occurred suddenly six weeks after admission to the hospital

A similar happening is shown in Fig 65 This patient was a white female

of 36 who had suffered from rheumatic heart disease since the age of seven During the last eight years of her life breaks in compensation occurred associated with recurrences of the rheumatic infection She showed excellent response to the usual therapy and was able to carry on her work until the



Fig 65 Rheumatic heart disease with mitral stenosis A massive thrombus occupies the whole of the dilated left auricle (Autopsy No 31 699 Philadelphia General Hospital)

day she was admitted to the Philadelphia General Hospital Death occurred suddenly and unexpectedly seven hours after admission and autopsy showed advanced mitral stenosis and a greatly distended left auricle entirely filled with thrombus which was white in the center and reddened at the periphery There were concentric laminations The entire thrombus meas

ured 5 × 6 × 8 cm Rarely these masses of clot may undergo complete organization with the formation of either pedunculated or ball valve thrombi (Fig 66) Occasionally these smooth loose bodies are discovered at postmortem in the auricular chamber always larger than the stenosed mitral orifice which they may at times acutely obstruct[9] In some patients this intermittent obstruction may give rise to characteristic symptoms that arouse suspicion of the presence of a ball valve thrombus Changes in the circulation in both upper and lower extremities may take place and progress rapidly to the formation of small areas

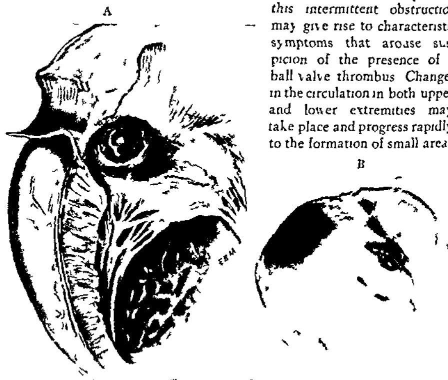



Fig 66 A Ball thrombus in left auricle
B Ball valve thrombus

of gangrene in the fingers and toes Full restoration of the circulation in these areas may occur suddenly if the pressure of the ball thrombus is released in which event the color and temperature of the arms and legs quickly return to normal Syncopal attacks may appear when a ball valve thrombus occludes the valvular orifice and sudden death is always a possibility

### Rheumatic Heart Disease of Long Duration Complicated by Auricular Fibrillation Pulmonary Emboli and Attacks of Paroxysmal Dyspnea

**Case 15** Mrs M J an American housewife of 51 was first seen in December 1937 complaining of palpitation and dyspnea

History The patient was well until two years prior to the first examination when dyspnea appeared on exertion About the same time she noticed palpitation and slight ankle edema in the evening There had been a 40 pound weight loss since the onset of illness At the age of 10 she had her first attack of rheumatic fever and was confined to bed for two months

PHYSICAL EXAMINATION B P 150/80 Puls rate 100 Rhythm totally irregular Slight cyanosis and mod rate ankle edema

Heart marked enlargement by percussion both to the right and to the left The apex impulse was palpable in the sixth interspace in the anterior axillary line There was a blowing systolic murmur and a mid diastolic rumbling murmur heard over the apex A systolic murmur was heard over the aortic area

LABORATORY DATA Blood count hemoglobin 82 per cent (Sahli) R B C 3 800 000 W B C 8 000 Wassermann negative

The electrocardiogram showed auricular fibrillation (Fig 67B) The roentgenogram showed cardiac enlargement in all diameters (Fig 67A)




FIG 67 A Roentgen film of chest There is cardiac enlargement with mitralization Note the congestion of the pulmonary vessels and multiple pulmonary infarcts B Auricular fibrillation The ventricular rate is well controlled by digitalis The action of this drug is also evident in the depression of the S T Intervals in leads 2 and 3

DISCUSSION The weight loss described by this patient was evident on physical examination Not infrequently patients with a long standing cardiac lesion will show loss of weight following anorexia that attends congestion in the portal system In others, the poor blood supply may interfere with proper nutrition of essential structures and wasting gradually appears (cardiac cachexia)

Treatment of this patient was begun by two weeks bed rest During this time she was digitalized and the ventricular rate reduced to 70 She was then allowed to be out of bed and about the house The dyspnea improved and the edema did not recur The dyspnea always returned however when further activity was permitted but on a markedly restricted program and maintenance digitalis she was kept fairly comfortable for a year

In December 1938 mild spells of paroxysmal dyspnea appeared following excitement or more than the usual amount of exercise McGinn and White [47] attribute these spells of pulmonary congestion that appear in patients with mitral stenosis to the strength of the right ventricle which in

certain situations pumps more blood into the lungs than can be passed through the mitral valve in time to prevent a stasis Evidence of the congested state of the lungs is furnished on these occasions by the appearance of rales and frothy bloody sputum If the right ventricle does not bear up under the increased load congestion often follows in the portal system with cyanosis large liver, and edema

These paroxysms became more frequent and distressing during the next few months The more severe attacks were controlled by injections of morphine sulfate 0 015 Gm (¼ grain) Finally during one of the seizures the patient developed a sharp chest pain that was followed by hemoptysis Dyspnea and other signs of congestive failure appeared on the scene very promptly No doubt the slowing of the blood current in the lungs produced by the delay in emptying favored thrombosis The resulting infarct was a large one judging by the extent of the physical signs that were evident a few days later in the left lower chest During the next six weeks there were two additional attacks of pulmonary thrombosis similar to the one just described Each occurred as the patient was showing some improvement in breathing and other signs of congestive failure

Following the last attack injections of mercupurin were given every fifth day regardless of the presence of visible edema Ammonium chloride was started at the same time and continued in 1 0 Gm (15 grains) doses after meals Improvement now was gradual but was maintained and the patient managed to regain her former level of exercise tolerance Following this restricted program and continuing the digitalis and diuretic maintenance dosage the patient has had no recurrence of her pulmonary symptoms for over a year and a half

## Rheumatic Heart Disease with Mitral Stenosis—the Influence of Hypertension on the Course of the Disease

**Case 16** Mrs F W a housewife of 55 was first seen in June 1937 at which time she complained of shortness of breath palpitation and edema These symptoms had all been present and increasing in severity for four months The patient had two attacks of rheumatic fever in childhood In 1930 a subtotal thyroidectomy was performed because of palpitation nervousness and loss of weight

Physical Examination Blood pressure 60/110 Dyspnea cyanosis and edema of both legs to the knees were present and there was marked distention of the jugular veins

Heart totally irregular rhythm rate 1 0 The left base measured 13 5 cm and the right 4 0 cm There was an accentuation of the first sound over the apex and a mid diastolic murmur There was a systolic murmur as well as an accentuation of the second sound over the aortic area There were no thrills palpable The liver was enlarged to the umbilicus Rales were present in both lung bases

Laboratory Data Wassermann negative Urine showed a trace of albumin and a fixed specific gravity of 1 010 on several occasions Blood count normal Basal metabolic rate plus 7 per cent

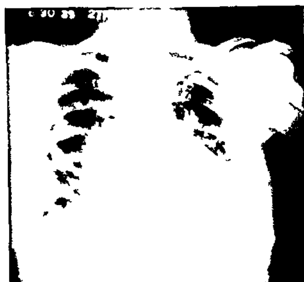
The electrocardiogram showed on first examination a rapid auricular fibrillation (Fig 68B) Digitalis reduced the rate and inverted the S-T intervals

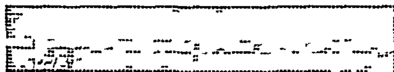
The roentgenogram (Fig 68A) showed enlargement of all cardiac diameters

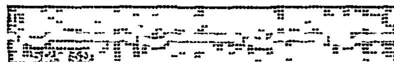
Clinical Diagnosis A Etiologic Rheumatic (Inactive) Hypertension B Anatomic Cardiac hypertrophy Mitral stenosis Mitral regurgitation C Physiologic Auricular

fibrillation Congestive cardiac failure D Functional Classification Class 3 Therapeutic Classification Class E

A







B

Fig 68 A Roentgen film Note marked cardiac enlargement all diameters
B The first strip (lead 1) taken 6/27/37 shows presence of auricular fibrillation The second strip (same lead) taken 5/26/39 shows a marked slowing of the ventricular rate to 58 with inversion of S-T intervals

Discussion The course of the rheumatic heart disease in this patient was complicated first of all by the appearance of thyrotoxicosis at the age of 48 She developed palpitation and dyspnea a slight enlargement of the thyroid exophthalmos tremor nervousness and loss of weight The basal metabolic rate was plus 45

Following a subtotal thyroidectomy the cardiac symptoms were much improved and her exercise tolerance increased During the next seven

years there was a gain in weight of 25 pounds In 1936 before the cardiac symptoms reappeared, the patient was told by her physician that she had high blood pressure

In 1937, her blood pressure measured 260/110 and mild congestive failure was present She was digitalized and proper maintenance dosage continued and in addition she was given elixir of phenobarbital, 4 cc (one dram) after meals A program regulating her daily activities which included a part time maid in the household, a two hour rest period every afternoon and ten hours in bed at night was prescribed A diet only slightly higher than her basal requirements was advised

For nearly three years her status has remained unchanged The heart is still greatly enlarged (Fig 68A) but she has managed to be about on *the same restricted program although the slightest increase in activity* causes marked dyspnea

Over half of the patients who have mitral stenosis develop high blood pressure when they pass the age of 45 which is an interesting fact when we consider that the blood pressures of the younger patients with mitral stenosis tend to be subnormal Does the long standing rheumatic disease produce organic changes that eventually result in hypertension? Certainly the mitral lesion in these patients cannot be ascribed to the hypertension since stenosis of this valve is never produced by an arteriosclerotic process

It is a very remarkable fact that the blood pressure in this patient is continually maintained at levels well over 200 systolic in the presence of an advanced mitral stenotic lesion However there is no reason why the factor that produces hypertension cannot be operative when the patient with the proper hereditary background reaches the age of 45 irrespective of the presence of a mitral stenosis

Levine s observations [18] indicate that the development of hypertension may actually be a helpful mechanism in these patients who have mitral stenosis He points to the fact that the majority of them have a life expectancy below 50 unless hypertension develops The hypertensive process dilates the left ventricle and this tends to counteract the effect of the rheumatic mitral lesion In this way there may be a balance restored between the mitral stenosis and the hypertension since the mitral lesion causes a right sided and the hypertension a left sided hypertrophy Consequently when failure arises from a prolonged strain on the right side of the heart in mitral stenosis, the beneficial effect of a process tending to produce a left sided hypertrophy can be understood

## Rheumatic Heart Disease with Lesions of All Valves—Prolonged Course of Therapy—Autopsy

Case 17 Mrs I M a white housewife of 40 had many hospital admissions over the course of five years because of recurring attacks of congestive failure Her chief complaints were shortness of breath and swelling of the abdomen There was no history of rheumatic fever in childhood

PHYSICAL EXAMINATION There was marked dyspnea slight cyanosis and ascites The latter increased in amount on each admission Toward the end abdominal taps were performed every second week and the average amount of fluid removed was 5000 cc On the last admission there was also fluid in the right pleural cavity

The heart showed considerable hypertrophy The right base measured 5 0 cm and the left 14 0 cm Systolic thrills and systolic and diastolic murmurs were present over the aortic pulmonic and mitral areas The rhythm was totally irregular with a rate of 100 to 1 0 B P 108/80

CLINICAL DIAGNOSIS A Etiologic Rheumatic Inactive B Anatomic Cardiac enlargement Mitral aortic and pulmonic regurgitation and stenosis C Physiologic Congestive cardia failure Auricular fibrillation D Functional Classification Class 4 Therapeutic Classification Class E

AUTOPSY Dilatation of the heart especially of the auricles The right ventricle occupied the entire ventral surface of the heart The coronaries were normal The mural endocardium was thick white and opaque in the auricles The mitral valve showed typical fish mouth orifice with greatly thickened valve leaflets The auricular surface was studded with calcific excrescences the size of a pin head and organized vegetations The papillary muscle was fibrosed The aortic cusps were shortened and thickened with dense adhesions at the commissures creating marked stenosis and insufficiency (Fig 69A) Moderate stenosis was present at the pulmonic valve and the cusps presented rolled edges slightly adherent to the commissures (Fig 69B) The tricuspid valve leaflets were thickened and densely adherent with the free edges rolled The chordae tendinae were shortened and thickened

DISCUSSION Involvement of all the valves of the heart is rare When an organic tricuspid lesion is present the mitral and aortic valves are usually the seat of advanced changes consequently it is often difficult to evaluate the effects of the tricuspid regurgitation and stenosis on the heart

In this patient separate thrills and murmurs were recognized over the mitral aortic and pulmonic areas but the findings as is quite often the case were confusing over the tricuspid area Systolic and diastolic murmurs were heard over the lower end of the sternum but it was felt that these were transmitted from the mitral area When more than one valve of the heart is damaged by the rheumatic infection the valves on the left side of the heart are as a general rule involved earlier and to a greater degree than those on the right side The order of frequency is usually mitral aortic tricuspid and pulmonic

The course of the disease in this case was typical [106] Hospitalization was required many times during the five years that symptoms were present The patient received active treatment on each occasion and sufficient circulatory balance was restored in a short time to permit her discharge However she did not follow a strict regime between admissions There was always a mild degree of congestion present The easily provoked dyspnea the mild cyanosis the distended jugulars the marked ascites and the chronically engorged and pulsating liver should have suggested a tricuspid lesion The auricular fibrillation present in this case was also consistent with the diagnosis

Between attacks of congestive failure these advanced circulatory alterations caused the patient very little discomfort Her margin was a very slim one and the balance difficult to maintain since the slightest over

exertion very quickly accentuated the cyanosis, dyspnea and other evidences of venous stasis

The management of a patient of this type is described on page 112

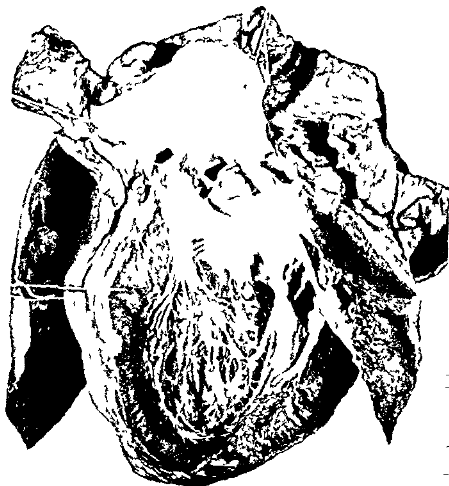


FIG 69 A Rheumatic heart disease Note marked distortion of the aortic cusps (Autopsy No 7 944 Philadelphia General Hospital)

## Rheumatic Heart Disease and Central Nervous System Syphilis—Management

**Case 18** L H an American salesman of 3? was first seen on March 30 1939 complaining of increasing shortness of breath and dull pain over the heart of six months duration For the past two *months he noticed occasional shooting pains in the legs* and nervousness The past history was negative for rheumatism Chancre at the age of ?0

PHYSICAL EXAMINATION showed irregular pupils; the right was larger than the left but both failed to react to light ALL SUPERFICIAL REFLEXES WERE ABSENT EVEN UPON REINFORCEMENT

Heart Enlarged L.B 11 5 cm from the midclavicular line R ght base 3 0 cm from M C L Rough systolic and long rumbling diastolic murmurs were heard over the apex A louder than P Thrill at the apex Rhythm regular (Fig 70 A)



FIG 69 B Chronic rheumatic endocarditis of the pulmonary valve Note thick n d r ll l d_ges slightly adherent t o mmissur s (A top s No 7 944 Philadelphi General Hospital)

LABORATORY DATA Blood and spinal fluid Wassermann reactions positive Electrocardiogram (Fig 70B) showed widened P waves other ise normal

CLINICAL DIAGNOSIS Central nervous system syphilis Rheumatic heart disease with cardiac enlargement and mitral stenosis

**Discussion** Although at times rheumatic may be mistaken for syphilitic aortic disease (Case 30) and in some instances it may be impossible to

determine the exact cause of regurgitation at the aortic orifice (Case 27), this patient should have caused no diagnostic difficulty

In the first place the physical signs elicited on cardiac examination point to involvement of the mitral valve since an apical diastolic murmur accompanied by a sharp snapping first sound are usually characteristic of

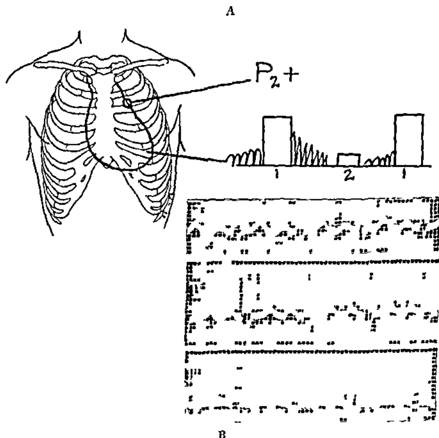



Fig 70 A Chart showing type and location of murmurs
B The electrocardiogram Note increase in the duration of the P waves

mitral stenosis This lesion is always rheumatic Diastolic murmurs at the apex may at times be associated with a syphilitic aortic regurgitation (Austin Flint murmur) In these cases the first sound of the heart will lack the snapping quality of mitral stenosis and the evidence of a marked aortic regurgitation will also be present

Again the age of the patient is a point in favor of the diagnosis of rheumatic heart disease Although it is possible to have clinical signs of cardiovascular syphilis at this patient s age the majority of cases are seen after 35

The presence of a definite history of syphilitic infection and the absence of a rheumatic history are both compatible with the diagnosis of rheumatic heart disease since about 50 per cent of the patients of this age who have established mitral stenosis will not give a history of any form of rheumatic infection

It may be possible that there is a combination of syphilitic and rheumatic heart disease in this patient, for this association is now believed to be a little more common than was once thought However we have nothing whatsoever upon which to base the diagnosis of syphilitic involvement in the absence of both systolic and diastolic murmurs over the aortic area The aortic second sound is not accentuated, and careful fluoroscopic examination shows the aortic diameter is not increased There is likewise no increase in the density of the aorta

At the present time there is no treatment required for the heart From the standpoint of the syphilitic infection the evidence points to the need of immediate treatment designed to prevent the progress of this disease in the central nervous system This is quite different from the plan that should be outlined when the cardiac study suggests an early spirochetal invasion consequently an understanding of the findings and prompt recognition of the type of heart disease present are extremely important

Under proper therapy for neurosyphilis this patient's progress should be good Careful routine cardiac studies should be carried out and future therapy directed toward protecting the cardiovascular system (page 214) This patient offers no cardiac contraindication to the use of pyrexial treatment for his neurosyphilis However in older patients with degenerative cardiovascular disease as the complicating lesion tryparsamide is the drug of choice

# 4

# PERICARDITIS

Pericarditis undoubtedly occurs more often than is recognized It may be acute or chronic involving only a small area of the pericardial sac and escaping clinical detection or it may be a readily recognized process demanding prompt and skillful management

## ACUTE PERICARDITIS

### Etiology

Pericarditis is usually encountered as a complication of some primary infectious process caused by pyogenic cocci (the *Pneumococcus Staphylococcus Streptococcus*) or the organism responsible for the acute rheumatic state While the pericardium may be the site of a primary invasion by the tubercle bacillus this organism more often arrives in the pericardium by extension from a neighboring focus The involvement of the pericardium encountered in uremia cancer and terminal conditions is probably not infectious although the exact cause is unknown in many cases Following a coronary occlusion involving the outer wall of the heart a local inflammatory area may develop in the adjacent pericardium Rarely trauma may be the exciting agent in pericarditis

Acute fibrinous pericarditis is most commonly seen as a complication of acute rheumatic fever and its frequency will depend on the incidence of rheumatic disease in the community A serofibrinous exudate may occur in all forms of pericarditis except those that complicate acute coronary occlusion and uremia In rheumatic infection the fluid that comprises the pericardial effusion is generally clear but may have a slight turbidity while following the invasion of pyogenic organisms a purulent pericardial exudate appears A bloody effusion (hemopericardium) suggests either malignant disease or tuberculosis Air may be present with the effusion (pneumopericardium) when perforation accompanies malignancy of a neighboring organ or it may enter from a pneumothorax or during a paracentesis

Acute pericarditis may be encountered in patients of any age but it is usually seen in young people because of the frequency of acute rheumatic infection at this time of life

### Pathology

When the pericardium is inflamed the membrane rapidly loses its glossy appearance owing to the changes that occur in the epithelial surface Fibrin then appears and the visceral and parietal layers may become adherent

although a solid union is usually prevented by the cardiac action When the layers of the pericardium are separated at autopsy the typical picture known as the bread and butter pericardium is observed (Fig 71) Healing may take place with only a thickening of the pericardium or in cases where the inflammatory process has been widespread adhesions may develop obliterating the pericardial sac or in rare cases anchoring the heart to neighboring structures

## Symptoms

When the inflammation extends from the pericardium to the diaphragm and pleura pain usually results This symptom may first call attention to



Fig 71 Acute fibrinous pericarditis (Hairy heart or cor villosum)

the chest and careful examination at this time will reveal a friction rub While this valuable sign may be absent its presence may remain undetected unless the physician is constantly alert and makes repeated examinations The friction sound is usually grating and harsh and appears to be nearer the ear than the ordinary heart murmur Firm pressure with the stethoscope may increase its intensity It is usually first heard toward the base of the heart and along the left sternal border and is present during

systole and diastole If loud this friction sound may be palpable The presence of a friction rub by no means rules out the possibility of fluid in the pericardial sac, although it usually disappears or becomes diminished in character when an effusion develops

### Signs

Accumulation of fluid in the pericardial sac in amounts in excess of 500 cc usually attracts attention to the heart The earliest sign can usually be detected by a roentgen study since bulgings first appear in the lower part of the cardiac silhouette These changes may also be observed by fluoroscopy As the effusion develops the area of cardiac dulness increases and additional signs become evident chief among which are the absence of cardiac pulsations under the fluoroscope and the characteristic shape of the cardiac silhouette (see Fig 25)

If fluid is present in large quantities it may compress the lung and produce an area of dulness in the left chest posteriorly just below the angle of the scapula Bronchial breathing will be heard over this area (**Ewart s sign**) *Unless pericardial effusion is kept in mind these physical signs including the elevated temperature and the dyspnea, suggest a diagnosis of pneumonia*

With further increase in the amount of fluid in the pericardial sac the heart sounds become muffled The return venous flow into the right auricle is hindered by the elevated intrapericardial pressure and distention of the jugulars and enlargement of the liver appear There is a fall in the blood pressure and pulse pressure During inspiration the radial pulse may dis appear (**pulsus paradoxus**) *As the venous pressure rises* the heart rate increases to compensate for the decreased diastolic filling The patient becomes cyanotic the veins in the neck are distended and liver engorge ment causes pain in the abdomen to appear there is a fall in the blood pressure and the respiratory rate is rapid The patient leans forward seeking relief This acute distress or **cardiac tamponade** is caused by large collections of fluid in the pericardial sac and calls for emergency treatment

### Paracentesis of the Pericardial Sac

*There are several methods of approach to the pericardial sac* and it is well to be acquainted with the technic of each one for in the event that adhesions block the approach to a fluid collection in one direction, another avenue may be employed successfully

Pioneers in this field recommended and used the epigastric route and considered it more practical and less dangerous Others use the fifth left *intercostal space about 2 cm inside the left border of percussion dulness* The pericardial sac may also be reached by passing the needle close to the sternum in the fifth left intercostal space to avoid the left internal mam mary artery (Fig 72)

**Technic** For the epigastric route the patient is placed in a r clining position preferably at an angle of about 30 degrees with his back well supported The skin to the left of the xiphoid is sterilized with iodine and infiltrated with a 1 per cent procaine solution A 20 gauge 3½ inch ne dle is used attached directly or by means of a flexible piece of rubber tubing to a 100 cc syringe The latter is preferable The insertion of the needle is in an upward and inward direction for a distance of approximately 2½ inches (Fig 73) depend ng upon the build of the patient and th thickness of the layer

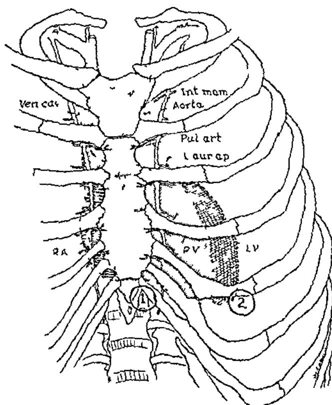
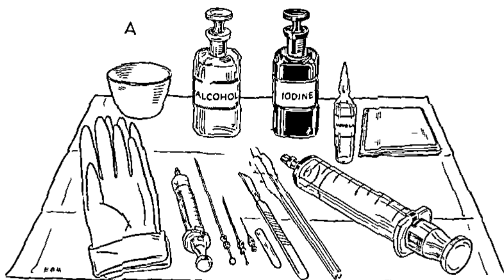
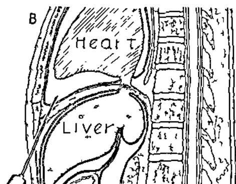



FIG 2 Diagram sho ing course of the internal mammary artery and the sites for *puncture of the pericardial sac*

of subcutaneous fat The needle enters the pericardium just above the diaphragm from *which point on good dependent drainage may be read ly obtained* If necessary the s me site may be used for drainage by res ct on of portions of the fifth and sixth cart lages *It is log cal to drain an effu ion from its lowest position belo v the heart; there are no vessels to cause conce n in the area traversed by the exploring needle* and the pleural and periton al surfaces are avo ded The advantages of the piga tric route are all the more evident if purulent pericardial collect *ons are su pected*

If the *anterior* approach is used th best point to enter is in the fifth interspace about *1 inch ns de* the outer bord r of card ac dulness Procaine solution should be nfiltrated carefully and the nee lle inserted slowly in a backward and upward d rection The needle *will be felt to enter the* per cardial sac when inserted about 3½ cm but this d st nce w ll again vary in accordance with the th ckne s of the subcutaneous tissues *In th s loca*



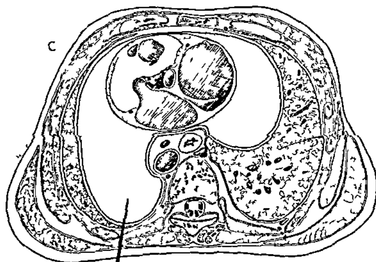




FIG 73 Pericardial paracentesis A Essential equipment B Epigastric approach C Posterior approach (See text for explanation )

tion it is well to use a blunt needle so that no harm may result if a coronary vessel is encountered If the heart is felt against the exploring needle this should cause no concern

Pericardial paracentesis may be carried out with the suction apparatus used for thoracentesis (see Fig 42) At times in the presence of tuberculous involvement when subsequent roentgen studies are to be made small quantities of air are injected into the pericardial sac following the removal of fluid The air outlines the sac sharply and in addition may be valuable in the treatment of the tuberculous process [191] However it is unlikely that the air is of importance in the prevention of subsequent adhesions in the pericardial sac (page 177)

Puncture of the pericardial sac is not a dangerous procedure when carried out with care If the first puncture does not reveal fluid the direction of the exploring needle should be changed If this approach is likewise unsuccessful the attempt should be made to enter the pericardial sac at one of the other sites described above I have often obtained fluid by using the epigastric route when the others have failed [306] In the presence of the dense adhesions that usually accompany tuberculosis of the pericardium the fluid may be encapsulated in which event attempts to reach it in one direction may be unsuccessful whereas large collections may be drained at another site of puncture (see Fig 79)

In children in whom an inflammatory process permits greater distention of the pericardial sac the lung may be pushed to one side or displaced and the pericardial surface will come in contact with the chest wall posteriorly If characteristic signs developed posteriorly this region should be selected for puncture (see Fig 73C) Williamson[404 405] recommends that pericardial paracentesis should be used more often to relieve discomfort and guard the patient against the danger of sudden death He uses the blood pressure changes as a guide Sutton[306] likewise recommends frequent tappings of the pericardial sac by the posterior route and shows that it is possible to carry out the procedure without passage through lung tissue If the posterior route is used the needle should be inserted in the center of the area of bronchial breathing usually about the eighth intercostal space (although the ninth or seventh interspaces may also be used) a little nearer the axilla than the spine Since the fluid obtained is usually thick and coagulates quickly a large bore needle is recommended

### Surgical Drainage

(See page 174)

## TUBERCULOUS PERICARDITIS

(See page 175)

## ILLUSTRATIVE CASES

### Acute Fibrinous Pericarditis During the Course of a Rheumatic Infection

**Case 19** F R a 10 year-old school girl was admitted to the Woman s College Hospital on May 6 1936 complaining of dyspnea and fever

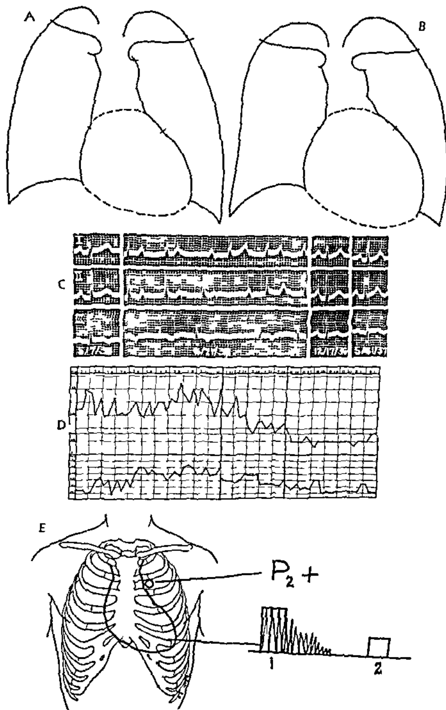



FIG 74 A The orthodiagram at time of discharge (September 1 1936) Note cardiac enlargement chiefly left ventricular B Six months later Note increase in heart size and mitralization

C The electrocardiogram (For explanation see text)

D The temperature and pulse record

E Chart representing clinical findings

HISTORY Acute rheumatic fever two years prior to admission The patient returned to school in two months and was well until the spring of 1936 At this time she visited her family physician who said that she was anemic and underweight and ordered the extraction of several teeth Two weeks following this pro edure fever was present every evening A week before admission there was malaise and soreness in the muscles of the legs and the patient was forced to remain in bed When the fever increased and dyspnea developed she was sent to the hospital

PHYSICAL EXAMINATION showed a pale underweight child of 10 suffering from moderate dyspnea T 10 P 130 R 35 B P 110/80 Jugulars not d stended The apex impulse was 1 cm outside the midclavicular line No thrills There was a musical systolic murmur over the mitral area The liver as not palp ble No edema

LABORATORY DATA Blood count hemoglobin 60 per cent (Sahli) R B C 3 400 000 W B C 16 000 differential P 80 L 0 The electrocard ogram on 5/7/36 (Fig 74C) showed slight elevation of the S T intervals in lead and 3

CLINICAL DIAGNOSIS A Et ologic Rheumatic Inactive B Anatomic Cardiac enlargement Mitral regurgitation Mitral stenosis (?) Acute pericarditis (?) C Physio logic Sinus tachycardia D Functional Class fication Class 3 Th rapeutic Classification Class E

DISCUSSION At the time of the recurrence of the rheumatic infection this child should not have been allowed to continue at school Again anemia and underweight does not constitute a diagnosis although it is one very frequently made Needless to say the symptomatic treatment of iron and high caloric diet does not lead very far if the underlying rheumatic infection is not suspected and bed rest promptly instituted To add in ult to injury but no doubt with the thought in mind of aiding the anemia dental extractions were advised The operation precipitated the attack with a violence that forced the patient to bed and it may have been the time when more extensive cardiac invasion took place

When admitted to the hospital the child appeared acutely ill The degree of fever and the marked dyspnea suggested the diagnosis of pneumonia to the intern in the receiving ward An incorrect diagnosis of this type is made more readily when a pericardial effusion compresses the left lung The appearance of an area of dulness in the left chest below the angle of the scapula over which bronchial breathing can often be heard may confuse the picture further Levine [18] suggests that this syndrome may explain the frequent history of childhood pneumonia in rheumatic patients

However this patient s lungs were clear at the time of admission and when the long history of fever was elicited the cardiac abnormalities helped to establish the diagnosis

The electrocardiogram showed a slight elevation of the S T segment but not enough to suggest the diagnosis of pericarditis * The P R intervals measured 0 2 second While this may be a perfectly normal conduction time in an adult 0 18 second should be viewed as the upper limit of normal in a child of this age

Two days following admission a friction rub was heard over the pre cordium and was especially loud along the left sternal border This was

* Elevat n of th S-T nte val should xceed 0 1 mv to be considered bnorm l

followed in 24 hours by further prolongation of the P-R intervals (Fig 74C) Frequent dropped beats were detected in the pulse and on auscultation over the precordium no premature beats could be heard during the pauses

The treatment for this patient during the first two days consisted of bed rest in the Fowler position and codeine sulfate 15 mg (¼ grain) by mouth every three hours for pain Since an ice bag over the precordium gave the patient considerable relief it was used continuously

The patient now appeared quite ill The pulse rate mounted with the temperature and the respirations became rapid and shallow In the presence of such an overwhelming cardiac infection digitalis was not given since no symptoms of congestive failure were evident The friction rub disappeared in 36 hours but the heart sounds remained distant although no other evidence of fluid accumulation in the pericardial sac appeared

With the disappearance of chest pain at the end of the first week acetyl salicylic acid 0 6 Gm (10 grains) with an equal amount of sodium bicarbonate were given every three hours in place of the codeine The heart rhythm became regular and the temperature curves approached lower levels (Fig 74D)

A more liberal diet was allowed as the temperature gradually returned to normal at the end of the fourth week At the end of the eighth week the patient was transferred to her home where she remained in bed another month under careful nursing care During this time she gained ten pounds in weight and had no recurrence of fever

When re examined in six months the electrocardiogram (Fig 74C) showed no conduction defect and the rheumatic infection appeared to be inactive However a faint diastolic murmur of aortic regurgitation was heard along the left sternal border although the pulse was not of the Corrigan type An orthodiagram at this time showed a well established mitral stenosis and cardiac enlargement (Fig 74B) The exercise tolerance of the patient was good although continued restriction had given her little opportunity for much exertion

This patient s history reveals the severity of the symptoms that usually accompany acute rheumatic pericarditis Extensive myocardial invasion was shown by the conduction defect that appeared in the electrocardiogram The endocardium by no means escaped since an aortic lesion was discovered at the follow up examination Evidence of the pericardial involvement appeared in the form of the friction rub that was audible for 36 hours All signs of pericardial involvement were absent at subsequent examinations although it is too early to state with certainty that a chronic pericarditis will not develop in later years While many still believe that rheumatism may be responsible for chronic constrictive pericarditis White[396] refers to a group of 100 children with chronic rheumatic heart disease followed over a 10 year period at the House of the Good Samaritan in Boston among whom not a single case of constrictive pericarditis has developed

## Acute Suppurative Pericarditis Secondary to Type II Pneumococcus Pneumonia—Drainage—Recovery

**Case 20** J V a Jewish girl of 13 was seen on 1/4/38 complaining of cough and fever

History Ten days prior to admission to the hospital the patient developed fever malaise and cough Four days later she had a chill followed by pain in the right lower chest and upper abdomen The pain was increased by breathing

Physical Examination T 101 P 130 Dyspnea marked Chest expansion was diminished on the right There was dulness to flatness in the right chest posteriorly below the angle of the scapula The breath sounds were diminished and there were crackling rales heard over the same area The vocal fremitus was markedly increased and the breath sounds in the left chest were exaggerated

The cardiac apex was in the fifth interspace in the midclavicular line The rhythm was regular No murmurs were heard There was tenderness over the right upper abdominal quadrant

Laboratory Data Blood count hemoglobin 80 per cent (Sahli) R B C 4 400 000 W B C 1 000 P 88 L 10 M Sputum pneumococcus type II

Roentgenogram (1/9/38) (Fig 75) showed a uniform density extending from the diaphragm to the fifth rib in the scapular line on the right side The heart and aorta were displaced slightly to the left The left lung was clear The changes present in the right lung indicated consolidation involving the lower and middle lobes In addition there was a moderate amount of free fluid in the right pleural cavity

Course These findings on admission indicated the presence of a type II lobar pneumonia Wide excursions of the temperature prompted us to aspirate the right chest on the seventh day Pus was obtained Consequently an incision was made under local anesthesia in the posterior axillary line paralleling the ninth rib The periosteum was stripped 1 inch of the rib removed the pleural cavity opened and a large quantity of pus evacuated A drainage tube was inserted

A week later the pulse rate began to rise and there was noted an increase in the cardiac dulness both to the left and to the right The heart sounds were distinct the first sound at the apex was split and a soft systolic murmur was heard in this region An area of percussion dulness appeared at the left base (Ewart s sign) a slight distention of the jugular veins was noted and this was followed by an increase in the respiratory rate A diagnosis of acute pneumococcic pericarditis was made

A roentgen ray examination at this time 1/18/38 (Fig 75) showed a pneumothorax on the right and a considerable increase in the size of the cardiac silhouette There were signs of fluid in the pericardial sac

Paracentesis of the pericardium (page 164) revealed 300 cc of a turbid fluid and a laboratory examination of the stained smear showed gram positive diplococci in pairs

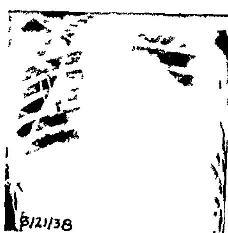
Discussion (Dr James Lehman) *—In this patient the pneumococcus invaded the pericardium from the empyema cavity Infectious processes below the diaphragm such as peritonitis abscess of the liver or pancreas ulcer of the stomach and subdiaphragmatic abscesses rarely extend to the pericardium

The symptoms that follow the involvement of the pericardium are variable and frequently are obscured by those of the underlying condition Consequently unless the complication is suspected and the symptoms searched for suppurative pericarditis may run its entire course without being recognized

The distinctive to and fro pericardial friction sound that has been

* Associate in Clinical Surgery Woman s Medical College of Pennsylvania













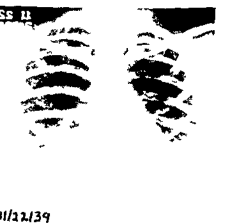



Fig 75 A Series of roentgen films taken during course of illness 1/9/38 Pneumonia with large pleural effusion 1/18/38 Pneumothorax following aspiration of large amount of fluid Collapse of the right lung 2/21/38 Enlargement of the cardiac silhouette Note the re expansion of the right lung 3/21/38 Drainage tube in pericardial sac 4/20/38 Cardiac shadow decreasing Patient discharged 11/22/39 Over a year later Heart smaller Physical condition of the patient excellent

described should always be sought at every examination I believe it may be heard during the early stages in nearly all cases When present it is missed most often because the integrity of the pericardial sac is not suspected so it should be a clinical rule to make frequent examinations of the precordial area in every case of pneumonia particularly if empyema has already developed

You will note from the history that this patient had some reference of pain to the abdomen At one stage abdominal tenderness was present Not infrequently pain referred to abdominal areas from a lower lobe pneumonia simulates an acute abdominal condition Sometimes in children a

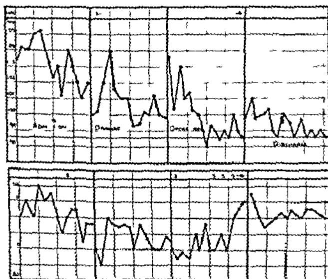


FIG 75 B Temperature and pulse record

pericardial involvement will produce pain in the abdomen that may be diffuse or it may be localized in the right lower quadrant and simulate acute appendicitis In many of these children most often rheumatic in type pain will also be referred to the neck or to the shoulder The development of the signs of pericardial involvement often clears the picture but sometimes the differentiation is not easy

When pericardial effusion increased in this patient typical signs developed Paracentesis of the pericardium revealed the presence of pus and indicated immediate surgical interference The operation of preference in these patients is resection of the fourth fifth and sixth ribs on the left side (Figs 76A and B) Adequate exposure is necessary Care should be taken first to avoid injury and contamination of the pleura and second to provide dependent drainage

The drain should be placed inside the pericardial sac so that all areas




Fig 76 Surgical drainage of the pericardial sac A Incision B Flap turned back and pericardium exposed

will be drained particularly the posterior section If a walled-off abscess is overlooked a fatality may result Gentle irrigation is not dangerous if small quantities of warm sterile physiologic saline are used in fact these may be quite necessary when the pus is thick and plugs of fibrin clog the drainage tube

If aspiration alone is used and operation delayed the mortality in acute suppurative pericarditis is 100 per cent If adequate drainage is established half of these patients survive Only 5 per cent of the cases that recover subsequently develop fatal adhesive pericarditis[339]

Following the adequate drainage of this child's pericardium and the subsequent use of sulfapyridine (see page 198) the temperature gradually returned to normal and the remainder of her convalescence was uneventful

A follow up examination nine months after discharge showed very slight thickening of the pleura at the base of the right chest with obliteration of the right costophrenic sulcus by adhesions (Fig 76) This portion of the chest therefore is almost normal and gives very little evidence of the extensive involvement that was present The heart is still displaced and slightly enlarged but its contour is normal The patient has no complaints and her exercise tolerance is good

## Tuberculosis Pericarditis—Autopsy

**Case 21** E A, a colored male of 31 was admitted to the Philadelphia General Hospital on 4/ 9/ complaining of cough shortness of breath and swelling of the legs

History The patient had attacks of pneumonia at the ages of ?0 7 and 30 Following the last attack he began to notice dyspnea and cough There was considerable weight loss Four months before admission swelling of the legs appeared and this was followed by a considerable increase in the dyspnea A month before admission the abdomen began to swell

Physical examination showed B P 116/80 dyspnea cyanosis and anasarca The heart rate was 90 the rhythm regular The heart sounds were weak and distant No murmurs were heard There were signs of fluid at both pulmonary bases A few crackling rales were heard over the left apex anteriorly Marked ascites was present

Laboratory Data Wassermann negative Blood count Hemoglobin 68 per cent (Sahli) R B C 3 ?00 000 W B C 7 00 differential normal Urine specific gravity 1 028 light cloud of albumin with a few hyaline casts

Electrocardiogram inverted T1 and T

Chest roentgenogram Bilateral pleural fluid

Course During the patient's stay in the hospital chest tap was performed 15 times and a total of 500 cc of pale amber fluid removed He gradually lost ground and died three months after admission

Clinical Diagnosis Pick's disease

Autopsy (Fig 77 ) Heart weight 1010 Gm The epicardium was markedly adherent to the pericardium There was a zone between the pericardium and the epicardium varying in width which contained communicating pockets that were filled with a cheesy material Here and there was a suggestion of the presence of the same material in the myocardium The muscle of the right auricular appendage showed definite tuberculous myocarditis The left lung showed moderately advanced fibro ulcerative tuberculosis

**Discussion** Tuberculous pericarditis is not a rare condition Since it occurs in about 5 per cent of autopsies on tuberculous subjects it may be

considered a disease of decided clinical importance While the mortality is high, healing may take place in some cases with the subsequent development of chronic constrictive pericarditis



Fig. 77 Tuberculous pericarditis and myocarditis (Autopsy No 7 50 *Philadelphia* General Hospital)

The pericardium may be invaded from foci in the lungs peritoneum pleura or mediastinal nodes The most common primary focus is the lung The patient whose history appears above i[illegible]mple of this type Very

rarely the pericardium is the only seat of involvement brought to light at autopsy Many cases thought to be examples of primary tuberculous pericarditis however may have an original focus so small that it is easily overlooked The infection of the pericardium in some cases may be part of a general miliary tuberculosis in which event it reaches the pericardium by way of the blood stream In the presence of a miliary tuberculosis the pericardial involvement is nearly always impossible to demonstrate clinically

Direct extension from the lungs is probably not as common an occurrence as invasion of the pericardium by way of the lymph channels that drain the mediastinal glands Symptoms arise during the course of this



A B

Fig 78 Tuberculous pericarditis

A Before paracentesis The cardiac silhouette is greatly enlarged due to collection of fluid in pericardial sac

B Following paracentesis of 900 cc and air injection Note small heart and thickened pericardial sac (Courtesy X Ray Department Philadelphia General Hospital )

involvement and lead to its detection for it may be ushered in by a friction rub In this respect it is not unlike the rheumatic variety The symptoms of the pulmonary disease may in some cases obscure this early sign in others no symptoms of any kind are present Effusion may attract attention particularly if it is large in which event dyspnea enters the picture The apex beat will no longer be palpable and the heart sounds will become distant and muffled and percussion of the chest will reveal a widened area of cardiac dulness Pulsus paradoxus appears if the effusion is large and bulging of the neck veins will be evident on inspection A paracentesis of the pericardium at this stage with the discovery of a hemorrhagic type of fluid arouses considerable suspicion concerning the nature of the process Success in the demonstration of tubercle bacilli in the effusion, either directly in the stained smear or following guinea pig inoculation will clinch the diagnosis

If air is injected into the pericardial sac following paracentesis (Fig 78) a small heart will usually be revealed surrounded by a very much thick

ened pericardium This appearance is characteristic of the lesion and is second in importance only to the finding of the tubercle bacillus

*Since no invasion of the endocardium occurs in tuberculous pericarditis no murmurs are usually heard* This may aid many times in differentiating tuberculous from rheumatic pericarditis since in the rheumatic state characteristic murmurs are nearly always present In acute rheumatism *there is a leukocytosis while in tuberculosis there is usually a normal white* blood cell count or even a leukopenia A higher temperature curve and a tendency to the appearance of congestive failure suggest rheumatic disease

Although in the early stages it may be difficult to differentiate between

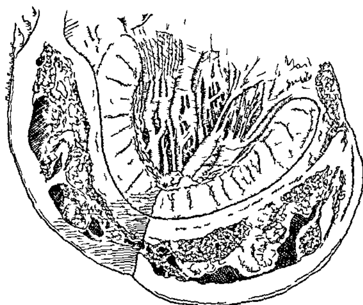


FIG 79 Tuberculous pericarditis Note the presence of exudate and adhesions between the thickened layers of pericardium

the acute rheumatic and the tuberculous forms of pericarditis subsequent happenings may make the distinction possible The rheumatic fibrinous exudate may disappear or pass into a chronic type with adhesions In *tuberculosis the pericardium becomes thickened the effusion becomes less* and masses of organized exudate remain between the layers of pericardium (Fig 79) Eventually adhesions may contract and this whole area may become obliterated with the development of a chronic fibrous process In the ashes of the fire no structure sufficiently characteristic to identify the original process as tuberculous may remain The absence of a rheumatic history or lesion and the presence of a tuberculous focus at another site in the body may be the only evidence that suggests the real nature of the initial process

In Fig 77 the tuberculous infiltration of the myocardium served to

establish the identity of the pericardial lesion The appearance of calcium in the healed pericardium does not establish the process as tuberculous since this type of infiltration often occurs in the healing of suppurative conditions

In tuberculosis of the pericardium larger amounts of fluid are recovered by paracentesis than in any other type The injection of air into the pericardial sac at the time of the tap was first suggested by Wenckebach in 1910 He replaced the fluid removed with half the volume of air and his patient showed much slower reaccumulation of the effusion Subsequent reports seemed to confirm this view and the first series of cases reported in the literature showed great symptomatic relief It is easier for the heart to work against air than a solid blanket of fluid and this decrease in *resistance may be responsible for the improved state of the circulation* Air however will not prevent the formation of adhesions in the sac as claimed by the original investigators in this field

The general measures used in the treatment of tuberculosis in other locations are also employed in tuberculous pericarditis Relief of intrapericardial pressure by tapping as often as necessary absolute bed rest and a high caloric diet constitute the essential points in the program Digitalis is rarely indicated since the symptoms of cardiac embarrassment are caused by the tamponade

If healing is accomplished and the signs of chronic constrictive pericarditis develop the only satisfactory treatment is surgical (page 184) The best results are obtained in young people who have no evidence of active infection

## CHRONIC PERICARDITIS

The resolution that follows acute pericarditis pursues a variable course depending on the type of the initial involvement and to a great extent upon the severity and duration of the process The clinical detection of chronic pericarditis is difficult for many times it produces no signs or symptoms and in the majority of the cases its presence does not influence the future health of the patient

### Signs and Symptoms

As healing of the pericardial lesion takes place *it quite often erases all* evidence of the nature of the primary process Consequently unless the past history of the patient is typical much confusion is bound to exist at the bedside or at postmortem in regard to etiology However evidence of rheumatic infection or tuberculosis elsewhere in the body may be of assistance while more rarely pneumonia coronary disease and malignancy must be considered as possible causes In the northern states rheumatic infection is found most often in the past histories of the patients presenting symptoms of chronic pericardial disease

The isolated patches of fibrous tissue in the pericardium pointed out as 'soldiers spots by the pathologist deserve only the passing interest that is usually given to them Even if definite adhesions exist between the layers of the pericardial sac no disturbance of cardiac function usually appears In fact in cases where adhesions are so numerous as to entirely obliterate the space between the two layers of pericardium, the heart may be un affected if adhesions to neighboring structures are absent

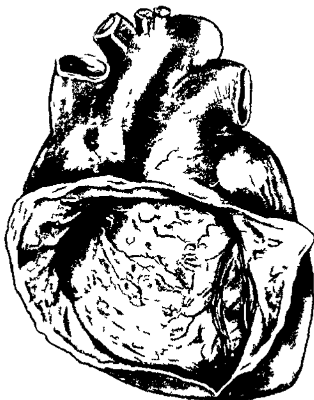


FIG 80 Chronic calcific pericarditi

**Constricting Adhesions and Chronic Tamponade** However if the healing process produces a thick layer of adhesions that entirely surround the heart cardiac action may in time be seriously compromised Contrac tion of these adhesions the unyielding character of which meanwhile may be considerably augmented by a widespread calcium (rarely bone) deposi tion not only interferes with the diastolic filling of the heart but also blocks venous return by constricting the lumen of the entering veins This condi tion is known as chronic constrictive pericarditis and is a feature of Pick's disease (Fig 80)

Adhesions may likewise develop between the pericardium and its con

tents and surrounding structures in the chest wall or mediastinum (chronic mediastinopericarditis) causing angulation or rotation of the heart and in consequence considerable serious interference with its action Recent views are not entirely in agreement with the old theory that cardiac traction is the cause of the grave sequelae when adhesions develop between the heart and neighboring structures Symptoms of importance arise only when adhesions either constrict the heart or cause its angulation or rotation by the formation of firm bands between the heart and neighboring structures

When adhesions constrict the heart and interfere with the venous return the liver enlarges Direct involvement of the hepatic vein may contribute to the severity of the process and ascites appears (Pick's mediastino pericarditic-pseudocirrhosis) The symptoms of chronic cardiac tamponade develop (Fig 81) It is much easier to remember these signs if the picture of compression of the heart is recalled instead of the old idea that the heart wears itself out to the point of failure by the added work of pulling against the adhesive bands **The triad of Beck** (1) a small quiet heart (2) a high venous pressure in the arm and (3) ascites and large liver[21] presents a brief summary of this condition and should facilitate the recognition of the disease

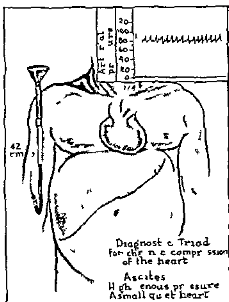



FIG 81 Chronic cardiac compression (Redrawn from Beck )*

* Reprinted by permission American Heart Journal

It can now be seen that the signs elicited on examination of the patient who has chronic pericarditis depend on the nature and distribution of the adhesive bands Unless previous rheumatic disease was present the heart will be normal and no murmurs will be heard If rheumatic involvement is present the characteristic murmurs and cardiac enlargement may be detected Usually the compressed heart of chronic pericarditis is small and under the fluoroscope its pulsations are not in evidence If adhesions have securely anchored the heart no change in position will be seen to follow the respiratory excursions The same fixation may be demonstrated on physical examination In some instances where the heart is firmly anchored to the chest wall by adhesions a systolic retraction of this area usually in the eleventh posterior interspace may be seen (Broadbent's sign)

## TREATMENT

The treatment of chronic pericarditis rests upon a careful estimation of the amount of embarrassment of the circulation that is produced by the adhesions [8 30] The effect of previous rheumatic disease on the symptoms of congestion must likewise be evaluated If tuberculosis subacute bacterial endocarditis or other infections are present the degree of their activity should be determined for operation in the presence of any active infection invariably leads to a poor result If the heart was normal before the adhesions developed operation may restore complete cardiac function for an indefinite period The most favorable cases for operation are young individuals presenting the triad of Beck who show no other evidence of heart or vascular disease

## CHRONIC CARDIAC COMPRESSION

(See page 180)

## ILLUSTRATIVE CASES

### Chronic Constrictive Pericarditis [13]

**Case 22** R F a white school boy of 12 was admitted to the Woman s College Hospital on 5/5/36 complaining of swelling of the abdomen

History Three years before admission the parents first noticed this swelling which gradually became worse until weekly tappings were required Dyspnea and cyanosis on exertion were noted Slight edema of the feet was present three weeks before admission No history of rheumatic infection A maternal grandfather had tuberculosis

Physical Examination Slightly emaciated boy of 1 years B P 90/60 Dyspnea Swelling of the veins of the neck No cardiac enlargement Fixed apex beat No systolic retraction Apical systolic murmur Lungs showed evidence of fluid at the right base Marked ascites The liver was felt 9 cm below the costal margin after tapping

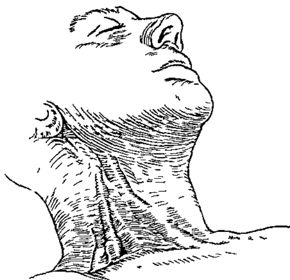
Laboratory Data Roentgenogram showed heart only slightly enlarged Lateral view showed a shell of calcium encasing the heart (Fig 8 C)

The electrocardiogram showed on first examination (See Fig 254A) notched P waves diphasic T and inverted T3 Examination two years later showed decreased voltage of the QRS groups and flat T waves

Clinical Diagnosis A Etiologic Unknown B Anatomic Constrictive pericarditis C Physiologic Restricted diastolic filling N S R D Functional Classification Class 4 Therapeutic Classification Class F

**Discussion** This patient when first examined showed ascites and signs of venous obstruction out of proportion to the amount of cardiac damage that could be demonstrated on physical examination A rheumatic history and signs of organic valvular disease were conspicuously absent The heart was small and the lateral roentgen study (Fig 82) showed a shell of calcium surrounding the heart A comparison of the electrocardiograms (Fig 254) revealed a decreasing amplitude of the QRS complexes and T waves that is so characteristic in these cases

Further studies showed a diminished cardiac output per beat and per minute and a decrease in the velocity of the blood flow The small heart



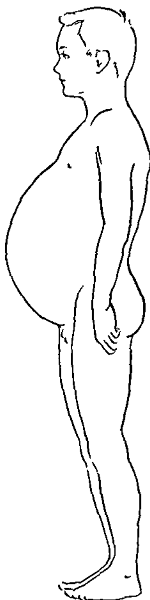







FIG. 8 A Swollen jugular veins
B Ascites
C Roentgen film (lateral view) Note layer of calcium encasing the heart

the decreased amplitude of the contraction evident on fluoroscopy and the shell of calcium in the roentgen film suggested that the cardiac symptoms in this child were due to decreased diastolic filling

In view of this explanation for the symptoms it was obvious that digitalis could contribute nothing to the plan of therapy Furthermore symptomatic medical treatment carelessly carried out in these cases may actually be harmful For example venesection performed for the cyanosis and bulging jugulars evident on slight exertion would dangerously lower the venous pressure to the point where it might be insufficient to accomplish auricular filling

The treatment indicated is pericardectomy The result will depend upon intelligent pre operative treatment and the experience of the surgeon The pre operative regime consists of limiting the fluid intake to 1200 cc daily and the sodium chloride content of the diet to 2 0 Gm daily The protein intake should be increased owing to the low serum protein that is generally encountered Mercurial diuretics are useful in the dehydration program that precedes operation Mercupurin is usually given in 2 cc amounts intravenously every three days with ammonium chloride in 1 0 Gm (15 grains) doses by mouth after meals Theobromine sodium acetate in 0 3 Gm (5 grains) doses after meals may be helpful between injections of the mercupurin

Thoracentesis (page 94) and abdominal tapping (page 96) were both indicated prior to operation in this patient Following the pericardectomy the diuretic drugs are continued until a complete cardiac balance is restored An intravenous injection of 2 cc of mercupurin every week for some months can be used to advantage and is not harmful

The operation of pericardectomy is usually carried out under ether anesthesia The second third fourth and fifth costal cartilages are resected on the left side The periosteum is left in place and this permits regeneration of the bony framework of the ribs following operation As much of the pericardium as possible is excised over both ventricles and the heart released from its constricting shell Relief is prompt striking and generally permanent

# 5

# ACUTE AND SUBACUTE BACTERIAL ENDOCARDITIS

Because all the sick do not recover does not prove that there is no art of medicine —CICERO *De Natura Deorum* Bk ii Ch 4 12

Bacterial endocarditis remains one of the saddest chapters in clinical medicine Whether it appears on the scene as a complication of an acute infectious process or whether it pursues a more insidious course after implantation upon a previously damaged heart valve the end result is the same In the first instance the disease is a rapidly fatal one in the second the duration of life may be a year rarely longer allowing the physician ample time to display his therapeutic skill Although the progress in treatment as far as final results are concerned has been slight with the continued improvement in our methods of attack the physician of tomorrow may witness the victory

## ACUTE BACTERIAL ENDOCARDITIS

Acute bacterial endocarditis is still referred to as malignant or ulcerative endocarditis The term ulcerative refers only to the pathologic change seen in the valves and gives no idea as to the nature of the etiologic agent Consequently the disease should be referred to as acute bacterial (pneumococcic streptococcic etc ) endocarditis using in the diagnosis whenever possible the name of the organism responsible for the lesion Acute endocardial lesions of a rheumatic nature are not included in this group

### Etiology

The organisms most commonly associated with acute bacterial endocarditis are *Streptococcus hemolyticus* (55 per cent) *Pneumococcus* (13 per cent) *Staphylococcus aureus* (12 per cent) *Gonococcus* (11 per cent) while miscellaneous invaders like the *Meningococcus* and the colon anthrax plague and pyocyaneus bacilli make up the remaining small percentage (Thayer) When these organisms are the active agents in the heart infection the clinical course covers but a few weeks If the duration of life is two months or over the condition is more apt to be due to *Streptococcus viridans* and is referred to as subacute bacterial endocarditis

### Pathology

Most of the bacteria that cause this fulminating type of infection are cocci They attack the heart by way of the blood stream to which they

gain entrance from a number of locations Common avenues of invasion include the uterine wall during the early puerperium the pneumonic lung wounds gonorrheal joints the meninges osteomyelitis boils and the infected pockets that remain following dental extractions Generally the organism gains easier foothold in previously damaged hearts lodging in most cases on the valvular structures although the endocardium is by no means immune to attack The vegetations that are products of bacterial growth may appear on the inner wall of the auricle or ventricle and along the intima of the aorta or a patent ductus arteriosus Their rapid growth gives rise to the appearance of ulceration and the heart valves or aorta may be so extensively invaded and weakened that aneurysmal pouchings (mycotic aneurysms) may soon appear Consequently rupture of these valve leaflets is not unusual

### Signs and Symptoms

**Vegetations** The persistence of the high fever of the original infection often tends to conceal the attack on the cardiac structures Blood cultures taken during the acute illness may have already detected and identified the invader in which event the question of cardiac involvement is often a matter of debate However if the patient lives and the endocardial vegetations increase in size two happenings call the clinician's attention to the heart First the growth of the vegetations on the aortic or mitral valve may change the character or pitch of a murmur previously noted If murmurs were absent one or more may now appear If these changes in the physical signs appear suddenly ulcerative processes should be suspected However the character or intensity of the murmur should never be regarded as an index of the severity of the process



Fig 83 Subacute bacterial endocarditis Petechiae on abdomen

**Embolism** The second happening is a more serious one Large (and usually infected) particles of the vegetations may break off form emboli and lodge in some distant organ (kidney spleen brain) with the production of metastatic abscesses Petechial hemorrhages into the skin may appear at this stage and may be regarded as manifestations of the same embolic process (Fig 83) In some cases none of these signs may appear in which event the cardiac complications are revealed only at autopsy

**Laboratory findings** aside from the positive blood culture give little

aid in detecting cardiac infection The leukocyte count is high and the urine may show a moderate amount of albumin and a few red blood cells to suggest a focal embolic lesion The electrocardiogram is negative unless the conduction system is directly invaded by extension from the endocardium which rarely if ever occurs

### Prognosis

In acute bacterial endocarditis embolism is usually the cause of death in a few days or weeks In other cases an overwhelming toxemia may hasten death before the inroads of the cardiac infection have been extensive Less often congestive failure appears as the terminal episode Fatal hemorrhages into the skin and mucous membranes or from the nose or gastro-intestinal tract may take place in some cases Recovery from this disease is most unusual but if it occurs chronic valvular disease will be the sequel

## ILLUSTRATIVE CASE

### Acute Bacterial (Gonococcal) Endocarditis Complicating Puerperium —Autopsy

**Case 23** W B a colored female of 18 was admitted to the Philadelphia General Hospital on 4/8/36 complaining of fever and pain in the left elbow of a week s duration She was pregnant at term

Physical Examination B P 150/100 T 101 F P 1 0 The rhythm was regular The apex beat was in the fifth interspace in the m dclavicular line There was a soft systolic murmur in the region of the cardiac apex

Laboratory Data Wassermann negative The ur ne shov ed a cloud of albumin and casts Blood count hemoglobin 71 per cent (Sahli) R B C 4 300 000 W B C 19 000 P 76 L 4

Course On 4/14/36 the patient was delivered spontaneously On 4/19/36 the blood cultu e was pos tive for gonococcus The septic temperature continued Death occurred on 4/24/36

Autopsy The heart weighed 350 Gm The septal leaflet of the aortic valve was ulcerated and necrotic and replaced by a soft m ss of grayish red f iable vegetations (Fig 84) The remaining leaflets were normal Along the line of closure of the mitral valve and on the au icular surface there was a single row of fresh vegetations which were easily broken off There was an ulcerat on on the m tral leaflet the size of a match head but no evidence of rheumatic valvul tis was present The tricuspid and pulmonic valves were normal

**Discussion** Considering the prevalence of gonorrhea gonococcal endocarditis is a rare complication In a recent publication Freund and his co workers were able to collect only 139 cases from the literature [109] Males predominated in their series and the age of the patients ranged from two to 51 years The average duration of the disease they found to be about ten weeks and the mortality 93 5 per cent

The diagnosis in this patient was established by blood culture and confirmed when the gonococcus was again recovered from the valve lesions at necropsy

There is at present no general agreement in regard to the plan of treatment that should be adopted in these cases In the few instances of recov

ery from the disease that are on record repeated transfusions, vaccines made up of killed gonococci antigonococcus serum and the intravenous administration of dyes constitute the measures employed However, we can



FIG 84 Acute bacterial (gonococcal) endocarditis of the aortic valve (Autopsy No 31 364 Philadelphia General Hospital )

safely say that all these therapeutic weapons have been used in many patients who did not recover

In the treatment of gonococcal arthritis and other systemic manifestations of the disease vaccines have enjoyed considerable reputation and acute reactions with temperature are essential to success Experimentally it has also been shown that nearly all the gonococci in cultures are killed

when exposed to a temperature of 106° F for four or five hours These facts form the basis of treatment by hyperthermia

Favorable reports have appeared recently in the literature where this type of therapy has been successful in gonococcal endocarditis and septicemia Williams[101, 40] using the Kettering hypertherm reports one case where fever treatment resulted in sterilization of the blood Healing lesions were found at autopsy and death was due to uremia and coexisting syphilis of the liver In another case reported as gonococcal endocarditis with gonococcal arthritis, fever treatment resulted in prompt recovery Freund and his co-workers report a cure in a negress of 20 following the use of fever therapy and recommend 106 7 to 107° F as the optimum temperature for gonococcal endocarditis However Hoyt and Warren[164] report a case treated for 17½ hours at 106° F where the result was fatal Krusen and Elkins[196] have also reported a case of gonococcemia with endocarditis treated by fever therapy without favorable effect

The possibility of a radical cure of the invasion by extirpation of the focus through which entry is gained into the blood stream is suggested by Wheeler and Connell who recommend hysterectomy

Today attention centers chiefly on sulfanilamide and its derivatives in the treatment of this disease Much has been written concerning the usefulness of these new drugs in gonococcal infections but opinion has not crystallized in regard to many essential points in therapy Long and Bliss [36] during the past few years have used sulfanilamide in two patients suffering from gonococcal endocarditis and bacteremia In both instances intensive therapy using doses suggested in Table V brought the endocarditis and bacteremia under control Both patients developed signs of acute nephritis during the course of their infection and in one death occurred from this complication One cure is reported following the use of sulfanilamide Long and Bliss point out the necessity of prolonged therapy if recurrences are to be avoided

At the present time the number of cases has been too small to permit a definite opinion as to the exact status of sulfanilamide therapy in acute bacterial endocarditis Other measures including frequent transfusions vaccines dyes and sera have been so uniformly unsuccessful that the hope of the future hinges largely on the success of the sulfanilamide group used either alone or in combination with pyrexial therapy

## SUBACUTE BACTERIAL ENDOCARDITIS

### Etiology

Subacute bacterial endocarditis is caused by organisms that show a less fulminating course after a foothold has been gained on a damaged valve leaflet but reveal an ultimate mortality that is comparable to the acute form Nonhemolytic *Streptococcus viridans* is the invader in the majority (90 per cent) of the cases The influenza bacillus the *Enterococcus* the *Meningococcus* and organisms of the *Brucella* group make up the remaining

percentage Very rarely higher bacteria (*Leptothrix* and *Actinomyces bovis*) invade the endocardial structures and produce a similar clinical picture

Subacute bacterial endocarditis occurs in about 1 to 2 per cent of all cardiac cases and in one out of every 25 to 50 cases of rheumatic heart disease Any vascularized scar in the endocardium appears to invite implantation of the *Streptococcus viridans* Consequently all congenital defects as well as arteriosclerotic and syphilitic valvular lesions, form potential sites Studies on a large series of cases[96, 68, 383] have shown that the *Streptococcus viridans* usually gains access to the blood stream from foci of infection in the upper respiratory tract and mouth Chronic otitic infections genito-urinary tract foci and open wounds should also be regarded as possible portals of entry The gastro-intestinal tract plays a minor role in spite of the many reports emphasizing the possibility of stasis with subsequent invasion from this area

It is not unusual to see cases of quiescent and well healed rheumatic endocarditis start their downhill course following an ill advised tonsillectomy or dental extraction Following these procedures the large areas in the mouth and throat covered by layers of necrotic tissue give ample opportunity to the ever present *Streptococcus viridans* to gain an easy entrance

## Pathology

When infection occurs the mitral valve is involved in the majority of instances but the aortic valve particularly if it is of the bicuspid type is not infrequently attacked (see Fig 126) The vegetations may also spread along the walls of the heart chamber invade the aorta and block the coronaries The *S viridans* also shows a great affinity for congenital defects of all kinds

When implantation occurs on a valve the inflammatory growth is again capable of extension into the valve with subsequent weakening of its structure and the formation of valvular aneurysms Vegetations break off and form emboli with the production of further complications in distant regions

## Signs and Symptoms

The symptoms of subacute bacterial endocarditis are much less severe than those of the acute variety that have just been described The onset *of subacute bacterial endocarditis is usually slow and so insidious that the* patient when seen is not able to give the exact date of the origin of his complaints At first a low grade fever with weakness loss of weight anorexia and joint and back pain is present Members of the patient's family or his business associates may notice the pallor and weight loss and suggest medical attention Tuberculosis malaria and other infections are apt to be suspected until a detailed study including a blood culture reveals the diagnosis Often an embolic episode may first cause the patient

to seek medical advice particularly if the embolus lodges in the region of the retinal artery or in an abdominal organ By the time that attention is directed to the source of trouble a palpable spleen clubbing of the fingers and marked anemia and all the signs that are so characteristic of the disease are usually present

**Murmurs** If no murmurs are audible care should be used in making the diagnosis If a murmur is already present following an old attack of rheumatic fever its features should be recorded and closely watched If the murmur changes in pitch or intensity during an interval between visits this may be considered as valuable evidence Crops of petechiae should be searched for each day (Fig 84) Tender fingers and toes as well as clubbing are other valuable aids in establishing the diagnosis

**Emboli** Repeated insults of an embolic nature may so decrease kidney function in patients with subacute bacterial endocarditis that uremic symptoms soon appear (Fig 85) Albuminuria and hematuria will appear before this terminal stage is reached and furnish a clue to the presence of renal disease

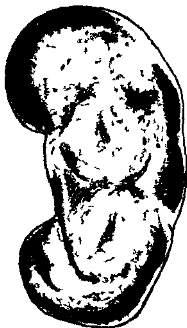


Fig 85 The kidney in subacute bacterial endocarditis Note the numerous petechiae and the scarring caused by multiple infarcts ( Flea bitten kidney )

**Heart failure** occurs more frequently in subacute bacterial endocarditis than is commonly believed a fact that has been brought out in a study by Buchbinder and Saphir[4] These observers likewise have shown that the heart in this disease is the seat of widespread anatomic changes consisting of minute emboli infarcts and abscesses and diffuse areas of inflammation with perivascular fibrosis These widespread changes are important to keep in mind when we formulate any plan of therapy

## Prognosis

If the opinions of all physicians who have treated subacute bacterial endocarditis were gathered a uniform hopelessness as to the outcome would be seen to prevail Once the diagnosis is firmly established I have never seen recovery take place Libman[30, 31] reports at least 3 per cent of recoveries in the usual type of the disease and believes that there is a possibility that more recoveries in mild cases occur but are overlooked These mild cases however are difficult to recognize Bacteria in the blood

stream may be few in number or absent altogether owing to their prompt destruction by the body forces of resistance as soon as they are swept from the vegetations If we view the matter from the angle of the postmortem examination evidence seems to be in favor of healing since the pathologist routinely encounters fibrosis and calcification in the structures that are involved in this disease

### Management

The management of these hopeless cases of subacute bacterial endocarditis is generally viewed by the practitioner as an ordeal that must be faced No other situation in medical practice surpasses it in testing the caliber of the physician These patients and their worried families require time thought tact and resourcefulness many times insisting on a trial of various remedies both old and new Continued failure often undermines confidence, and the physician becomes wearied and discouraged when he should remain watchful and hopeful At least we can keep hoping meanwhile guarding our patients against unnecessary and at times actually harmful measures A regime of therapy should be chosen that will encourage and aid the forces of Nature My therapeutic attempts and their uniformly poor results are reflected in the following case histories

## ILLUSTRATIVE CASES

(Showing Hyperpyrexial Therapy Transfusion Sulfanilamide, Sulfapyridine Heparinsulfapyridine Therapy and Arteriovenous Aneurysm Excision)

### Rheumatic Heart Disease—Subacute Bacterial Endocarditis

**Case 24** Mrs T F an American housewife of 30 was first seen on September 3 1936 There were no cardiovascular symptoms She was pregnant at the third month and her physician requested evaluation of a systolic apical murmur discovered on routine physical examination

The patient had one attack of rheumatic fever at the age of 1?

Physical Examination B P 108/80 Pulse 80 No irregularity A rough systolic murmur was heard over the apex transmitted well into the axilla The pulmonic second sound was accentuated Slight cardiac enlargement was present The electrocardiogram was normal

Clinical Diagnosis A Etiologic Rheumatic Inactive B Anatomic Slight cardiac enlargement Mitral insufficiency C Physiologic Normal sinus rhythm D Functional Classification Class I Therapeutic Classification Class B

The opinion was given that the pregnancy would not be complicated by any cardiac symptoms Routine examinations were advised (Chapter 15)

This patient was next seen on 9/16/38 Her pregnancy had been uneventful She was well until a month before the examination when she developed headaches weakness and slight dyspnea

Physical Examination Cardiac status unchanged The spleen was not palpable The blood count hemoglobin 90 per cent (Sahli); R B C 4 800 000 W B C 11 200 Blood culture negative

When re-examined one month later 10/16/38 the patient had lost eight pounds in weight Her complaints were weakness, palpitation and dyspnea The temperature was 99 3 F She was admitted to the hospital for study A week later the blood culture was positive for *Streptococcus viridans*

**Discussion** When the cause of this patient s symptoms was revealed by the positive blood culture she was ambulatory slightly overweight and appeared to be in good health The amount of cardiac damage resulting from one attack of rheumatic fever in childhood was slight and well healed She came through one pregnancy without complications was able to manage her household efficiently and took part in numerous outside activities

The development of subacute bacterial endocarditis in a young person of this type whose heart damage has been trivial and certainly compatible with a reasonable life expectancy is tragic and calls for heroic measures To give a hopeless prognosis on the basis of the blood culture to families of these patients is not an easy task particularly when the victims glow of health at the time is but slightly dimmed Newspaper and radio health talks that also bring to the fireside the news of wonderful advances in medical science have little to say regarding this disease However other well advertised scientific discoveries naturally lead relatives to expect that *surely something can be done*

Consequently when the S viridans was cultivated from the blood of this patient vaccines from the organism were prepared and injected into suitable donors in ascending doses in an attempt to procure immune blood Three robust donors were inoculated over the course of three weeks At the end of this period of preparation the blood serum of each agglutinated the S viridans in high titer During the patient s first month in the hospital ordinary transfusions of 500 cc of whole blood had been given every week There were no reactions and the blood count was kept at 5 000 000 During the fifth week transfusions from the immune donors were begun When 100 cc of the first transfusion had been injected so severe a reaction developed that the transfusion had to be discontinued Five days later only 50 cc of the blood drawn from the second donor were given before a similar marked reaction took place The patient refused to take the next transfusion and the third donor was not used

The failure of this therapeutic procedure was discouraging and the severity of the reactions experienced by this patient makes me hesitate to recommend it In addition the method is time-consuming and expensive and usually it is difficult to get professional donors to submit to injections of vaccine

Recently Kilgore[189] recorded three similar failures in cases where the amount of immune blood given exceeded that in any of the previously reported cases while Howell Portes and Beverley are more hopeful [163] Nevertheless their patient died a week after the last transfusion The improvement was temporary following each injection of the immune blood and may have been due to increase in the blood count or the agglutinins for the infecting organisms The possibility also exists that the effect was purely psychic

In addition to injections of immune blood Lamb gave serum from an immunized horse and reports an unfavorable result [90] Other accounts in

literature dealing with immune hemotherapy in subacute bacterial endocarditis are not enthusiastic[163, 199]

The use of the immune donor however, appeals to the representatives of the family They view the doctor as a modern Galahad fighting the microbe with strange and intricate weapons and as a result they have much to tell abroad The morale of everyone connected with the case enjoys a temporary elevation, which is reflected at once in the patient s attitude This is my impression of the value of immune hemotherapy

During the second month of this patient s stay in the hospital the steady downward course was evident Transfusions of whole blood were *used frequently but in spite of them the blood count fell to 54 per cent* hemoglobin, 2,300 000 red blood cells by the end of the eighth week Occasional embolic phenomena were now in evidence in the extremities (tender nodes) the kidneys (hematuria, backache) and the spleen (tenderness enlargement) Weight was lost rapidly and the degree of toxemia increased

Toward the middle of the third month a greater degree of cardiac enlargement was noted the liver became enlarged and tender and edema of the feet dyspnea and slight cyanosis appeared While these signs of heart failure are unusual in the cases of subacute bacterial endocarditis they may be explained by the fact that the patient escaped major embolic accidents as the months went b In this event it is only natural to suppose that the myocardium would become the seat of sufficient structural damage to account for its failure[4] Therefore it is evident that we need no longer make use of that indefinite term toxemia to explain the myocardial weakness and failure that develop in the course of subacute bacterial endocarditis Sudden rupture of a valve the seat of a mycotic aneurysm may add an additional load that precipitates failure in some instances

In the presence of fever and such extensive myocardial injury it is little wonder that no response was obtained when the patient was digitalized Vitamin $B_1$ (thiamin chloride) and C (cevitamic acid) were given in large amounts by mouth and parenterally when edema appeared with no obvious result An increasing stupor was soon replaced by coma and the patient died at the beginning of the thirteenth week

A postmortem examination was not obtained in this case nor was it requested There are times when the physician finds it impossible to go to willing co operative families with a last request of this nature particularly if he knows from the close contact of weeks that this debt to science if paid will immeasurably increase the burden of grief

### Subacute Bacterial Endocarditis—Insidious Onset and Long Duration —Autopsy

**Case 25** W W a white male physician of 34 was admitted to the Philadelphia General Hospital on 11 17/31 complaining of fever and loss of weight

History Over a year before admission the patient was awakened by a sudden severe backache radiating toward the left sacro iliac joint The pain was partially relieved by aspirin and he was able to attend to all the duties of his practice At the end of a week he consulted an orthopedic specialist who following a roentgen ray examination made

a diagnosis of osteoarthritis of the sacroiliac joints A belt was prescribed which gave the patient some relief although the backache continued to be troublesome

Headaches were then present every day and slight pallor was noticed by members of the family Consequently the doctor visited another colleague and had his glasses changed He also stopped by the hospital and had a blood count A moderate secondary anemia was found A vacation away from home was the prescription anemia and overwork the diagnosis

A month at the seashore was of little value On his return to the city a loss of five pounds in weight was noted There was a slight cough and an evening temperature as high as 100 F A chest specialist was consulted who found evidences of tuberculous infiltration at both apices and sent the patient home to bed Inquiry revealed that two brothers and one sister had died of tuberculosis

During the next four months at home little improvement was observed The temperature continued the anemia increased and the patient lost 26 pounds in weight

When admitted to the hospital the physical examination revealed pallor a temperature of 100 F a pulse of 80 and the blood pressure measured 96/84 There was dulness on percussion over both apices No rales were elicited The apex beat was in the sixth interspace just outside the midclavicular line and there was a harsh apical systolic murmur transmitted into the left axilla The fingers were clubbed

Laboratory Data Blood count hemoglobin 60 per cent (Sahli) R B C 3 000 000 W B C 17 000 *Wassermann reaction negative* Six sputum examinations were negative

At the end of the first week the blood culture was reported positive for *S viridans* The same day petechiae appeared in the conjunctivae and the spleen was palpable for the first time

Clinical Diagnosis A Etiologic Subacute bacterial endocarditis *S viridans* B Anatomic Slight cardiac enlargement Mitral regurgitation C Physiologic Normal sinus rhythm D Functional Classification Class 1 Therapeutic Classification Class E

*The course was slowly downhill and the patient died 12/14/31 15 months after the* onset of symptoms

Autopsy The heart weighed 300 Gm The pulmonic valve was normal The tricuspid valve showed a few vegetations about 1 to mm in diameter The left side of the heart (Fig 86) revealed extensive growth of vegetations on the free border of the mitral valve *extending down on the chordae tendineae and on the left auricular wall* The aortic valve was normal Both lungs revealed healed apical lesions of tuberculosis The spleen and kidneys showed multiple areas of infarction

**Discussion** The history of the onset of this patient s illness is typical of the disease Often vague joint pains and headaches occur as prodromal symptoms Fever may develop during the early stages and disappear for long intervals but it always recurs and once established seldom leaves the picture completely for any length of time

This patient s story brings out the danger of viewing pain in a location that happens to be the official precinct of a specialist as a result of a disease process at this site There is no doubt that a mild degree of osteoarthritis was present in the region indicated but the local findings in this case did not explain the whole picture The same observation holds true with regard to the headache The patient was a physician and for this reason his fellow practitioners took too much for granted when he consulted them in regard to a symptom It was quite natural when the history of tuberculosis in the family was revealed and the roentgen study showed bilateral apical shadows that the expert on chest should feel that the patient s case was fully solved and advise him accordingly We are all apt to develop blind spots for certain unexplained symptoms when we are either too tired or too hasty Unfortunately at a later date we may see

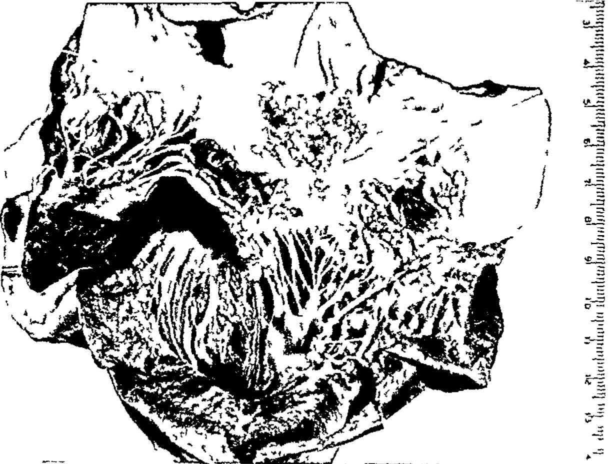


Fig 86 Subacute bacterial endocarditis Note the extensive growth of vegetations on the free border of the mitral valve the chordae tendinae and on the wall of the left ventricle (Autopsy No 3 663 Philadelphia General Hospital)

these symptoms develop to embarrassing proportions The flower in full bloom may be readily named by a colleague when its species is difficult to recognize in the bud

When this patient was viewed as a whole the parts of the puzzle went into place very readily The embolic manifestations were recognized and the positive blood culture clinched the diagnosis The autopsy showed an extensive growth of vegetations not only on the heart valve but also on the auricular wall The apical lesions of tuberculosis were found but they were completely healed The areas of infarction in the kidneys suggested another cause for the backache that ushered in the illness

### Subacute Bacterial Endocarditis Accompanied by Multiple Embolic Episodes—Autopsy

**Case 26** R F K a male clerk of 31 was admitted to a surgical service at the Woman s College Hospital on January 1935 complaining of sudden pain in the abdomen

History For two months following a dental extraction the patient had complained of weakness vertigo and headache and was unable to work for the week before adm ss on because of increase in the severity of the symptoms The past history showed attacks of rheumatic fever at the ages of 11 and 13

Physical Examination T 101 F P 110 B P 150/40 Pallor Corrigan pulse There was cardiac enlargement to the anterior axillary line The heart rhythm as regu lar There was an accentuation of the first heart sound at the apex and in the same area a diastolic thrill was palpable Presystolic and diastolic murmurs were heard in the m tral area Along the left sternal border there was a lou d diastolic murmur The spleen was palpable and tend r The fingers showed marked clubbing

Laboratory Data Blood cultures 1 5 colonies of *Streptococcus viridans* per cc of blood Wassermann reaction negative Blood count hemoglobin 55 per cent (Sahli) R B C 3 200 000 W B C 14 000 The urine showed 10 R B C per H P F

Clinical Diagno is A Etiologic Rheumatic Subacute bacterial endocard t s *S viri dans* B Anatomic Aortic insuffic ency M tral steno is M tral insufficiency C Physio logic Normal sinus rhythm D Functional Classificat on Class 3 Therapeutic Clas fica tion Class E

Discussion Needless to say this patient did not require surgical treat ment Viewing the history subsequent to the extraction of three teeth we cannot state that the development of subacute bacterial endocarditis was merely a coincidence I have many times seen the *S viridans* gain a foot hold in a previously damaged endocardium following an ill advised tonsil lectomy or dental extraction This patient had three teeth removed because of abscesses that were demonstrated on roentgen examination He was advised to have this done because of heart trouble A local anesthetic was injected which may have forced infected material lurking about the margins and roots of the teeth deep into the capillaries and given it a good start on its way to the heart valves

In all patients who have damaged hearts particularly the younger ones where rheumatic and congenital types predominate dental extractions should not be freely advised or carelessly undertaken A complete physical examination should first be carried out Anemia and dietary deficiencies brought to light should first be explained and then corrected by iron

vitamins and a proper diet This may help to increase those forces of resistance that we so often refer to in our daily practice

When the patient is ready to have the dental operation the surgeon should first give the teeth a thorough cleansing to remove the contaminants from the field Extractions should then be carried out at sensible intervals After each extraction a thorough cleaning of the socket is advisable and packing should be avoided if possible All patients known to have heart lesions should be referred first to their physician by the dentist before any operative work is begun in order that responsibility may be shared and all the protective measures employed

It seems likely that *S viridans* invades the blood stream of normal individuals many times during a lifetime This fact may often be demonstrated by the use of special technic [98, 311] I am not convinced that the endothelial structures are more permeable in late winter and spring and less permeable in summer and autumn and that we should confine our operations to these favorable seasons When we advise operations on teeth and tonsils at any season in patients known to have heart disease the use of sulfanilamide or one of its derivatives before and after the operation is worthy of trial to combat the transient bacteremia that often occurs

TABLE V

SULFANILAMIDE DOSAGE

The Amounts of Sulfanilamide Necessary to Establish Effective Blood Levels (10 to 15 Milligrams Per Cent) Quickly in Patients Ill with Severe Hemolytic Streptococcal Meningococcal Gonococcal Pneumococcal or Welch Bacillary Infections

| WEIGHT OF PATIENT | | INITIAL DOSE *Per Os* | | MAINTENANCE DOSE *Per Os* q 4 HOURS (DAY AND NIGHT) | | TOTAL DOSE FIRST 24 HOURS | | TOTAL DAILY DOSE BICARBONATE OF SODA | |
|---|---|---|---|---|---|---|---|---|---|
| KILOS | POUNDS | GRAMS | GRAINS | GRAMS | GRAINS | GRAMS PER KILO | GRAINS PER POUND | GRAMS | GRAINS |
| 70 | 150 | 4.8 | 80 | 1.2 | 20 | 0.15 | 1.2 | 3.6 | 60 |
| 60 | 125 | 4.2 | 70 | 0.9 | 15 | 0.15 | 1.2 | 3.0 | 50 |
| 45 | 100 | 3.6 | 60 | 0.9 | 15 | 0.18 | 1.3 | 3.0 | 50 |
| 35 | 75 | 3.6 | 60 | 0.9 | 15 | 0.23 | 1.8 | 3.0 | 50 |
| 23 | 50 | 3.0 | 50 | 0.6 | 10 | 0.26 | 2.0 | 1.8 | 30 |
| 11 | 25 | 1.8 | 30 | 0.3 | 5 | 0.30 | 2.2 | 0.9 | 15 |

From Long and Bliss Clinical Use of Sulfanilamide and Sulfapyridine and Allied Compounds —Reprinted by permission Macmillan Co N Y

When subacute bacterial endocarditis develops however the use of sulfanilamide derivatives alone have no effect on the course of the disease This patient was the first under my continuous care where sulfanilamide was used in an attempt to rout the invasion of the *S viridans* Very slightly lower doses were given than have since been recommended by Long and Bliss [36] *in Table V An initial dose of 4.0 Gm (60 grains)* of sulfanilamide was administered and this was followed by 1.0 Gm (15 grains) doses

every four hours accompanied by a similar amount of sodium bicarbonate. No untoward effect was noticed. During this week there were many variations in the temperature, but it is impossible to state whether they were due to the drug, since similar remissions occurred in the absence of sulfanilamide. Blood cultures were negative during the period in which sulfanilamide was given, but were positive again when the drug was discontinued, demonstrating the failure of the chemical to penetrate the depth of the lesions on the heart valves.

There are comparatively few reports in literature of large series of cases of subacute bacterial endocarditis treated with sulfanilamide. Isolated instances of recovery have been reported by Hussey[166] Major and Leger[2 4] One patient reported by the last observer was cured by combined sulfanilamide and neoprontosil therapy, but died of congestive failure 29 days later. Autopsy showed damage of the aortic and mitral valves, but cultures of removed segments were sterile. While the diagnosis in other reported cases of cure may be open to doubt, the patient reported by Major and Leger had a history of rheumatic fever and old mitral and aortic valvular lesions, petechiae, splinter hemorrhages, tender fingers, fever, enlargement of the spleen, and three blood cultures positive for *S viridans*. Necropsy showed the evidence of a recent endocarditis in the stage of healing and repair. The question of course arises whether or not cure was produced in this single instance by the use of the drug or whether it was another example of spontaneous recovery. We can be hopeful that it was an example of the efficacy of the early use of sulfanilamide before the bacteria in the valve lesions became inaccessible, since the time of the institution of sulfanilamide therapy in these cases appears to be a most important factor.

Spink and Crago[3 0] in a detailed evaluation of sulfanilamide therapy in 12 cases of subacute bacterial endocarditis report a bactericidal effect that was temporary and depended on continued use of the drug in 10 of the 12 instances. They conclude that the value of sulfanilamide is doubtful. Long and Bliss[36] have observed the effects of sulfanilamide in more than 60 cases of subacute bacterial endocarditis. They report five cures; in four of these patients the infection was engrafted on a congenital lesion and in the fifth case there was a rheumatic background.

I still give sulfanilamide to every patient under my care who is suffering from subacute bacterial endocarditis. If the drug is well borne I continue it in sufficient dosage to maintain the concentration of 10 to 15 mg per cent. I have always used sulfanilamide by mouth. The only tests of efficacy of this treatment are the blood cultures.*

Sulfapyridine gives the same results in subacute bacterial endocarditis as sulfanilamide. Bacterial growth disappears from the blood culture as soon as the drug is administered. In some cases this is attended by a fall

* All blood cultures for *Streptococcus viridans* should be incubated for at least 10 days before a negative report is made; this precaution is especially advisable when a chemotherapeutic agent is present in the blood sample.

in the temperature When the drug is withdrawn and in some cases while it is still being given all the clinical features of the disease return in much the same intensity as before Long and Bliss advise the use of a total daily dose of 0 1 Gm per kilogram of body weight in patients weighing up to 60 kilograms The dose should be divided and given at intervals of six hours

Kelson and White[183] have recently reported their experience in using sulfapyridine combined with heparin They call attention to the fact that the streptococci lie near the periphery of the vegetations embedded in fibrin and platelets that act as an efficient wall preventing the contact of leukocytes with the bacteria Heparin an anticoagulant is used to limit the growth of the vegetations to encourage fibroblastic invasion of the area and to prevent if possible embolic accidents that invariably follow the extensive thrombus formation

Technic of the method proposed by Kelson and White is as follows dissolve 10 cc of heparin (10 000 units) in 500 cc of physiologic saline and administer by uninterrupted intravenous drip day and night for 14 days The flow is regulated to maintain venous clotting time (normally below 20 minutes) at approximately one hour Clotting time must be determined before treatment, twice during the first day and then daily until the heparin is discontinued The sulfapyridine in suitable amounts is started (Table V) *from four to seven days before the heparin* and continued during the heparin treatment and for one week following its withdrawal Blood transfusions are given if the blood count falls below 3 500 000 red blood cells To increase the efficiency of fibrous repair the patient is saturated with vitamin C It is well to give 200 mg of cevitamic acid by mouth four times a day for three days and then continue it in daily doses of 100 mg

Three of the first six patients reported by Kelson and White who were able to take the heparin for more than a week showed striking improvement and have remained free of evidences of the disease for periods of ten weeks 18 weeks and four weeks respectively, after discontinuing treatment These afebrile intervals are much longer than usually occur in control cases

Certain dangers attend the use of heparin but these must always be viewed in the light of the hopeless prognosis that the disease invariably carries with it Two patients of this series had toxic reactions to the heparin death resulting in one case in 17 hours Another danger that must be considered with the use of heparin especially in a disease like subacute bacterial endocarditis is fatal hemorrhage due to interference with clotting following embolic episodes Friedman and his associates[108] emphasize this danger following heparin in their report of a single case where a fatal cerebral hemorrhage terminated the picture ten days after heparin was administered These authors also believe that some danger attends the sudden liberation of large quantities of bacteria when the vegetations are broken up

The final opinion in regard to the effect of heparin sulfapyridine therapy in subacute bacterial endocarditis must await the result of further careful clinical and laboratory studies Additional animal experiments must be carried out to prove the action of heparin in the concentrations recommended Does it actually prevent the deposition of platelets and fibrin on the valves as claimed? Will this action allow Nature to gain the upper hand and produce firm healing in these areas? These answers we hope




FIG 87 Subacute bacterial endocarditis Infarct of spleen following embolism

will soon be obtained Meanwhile every effort should be directed toward early diagnosis when the vegetations are fresh and small for only under these circumstances can we hope that this plan of attack will have the success that the early case reports have led us to expect

For the present it must not be assumed that a cure has been found My personal experience with heparin in subacute bacterial endocarditis has been most discouraging The dangers in my opinion are prohibitive even when we consider the nature of the disease this therapy has been fashioned to combat and they should always be explained to the patient s family before the treatment is begun Heparin should only be used in the

hospital where its effects can be constantly observed and the results appraised after an adequate follow up period

In the presentation of this new plan of chemotherapeutic attack with its many variations we have digressed for the moment from the case under discussion Embolic manifestations showed the same tendency to occur during the second week in fact were more frequent after sulfanilamide was begun On the tenth hospital day the patient died suddenly from what we considered was a massive cerebral embolism

The autopsy showed old rheumatic lesions of the mitral and aortic valves with large masses of vegetations in both locations A large splenic infarct (Fig 87) explained the abdominal pain that was present on admission Both kidneys showed the numerous scars and petechiae (see Fig 85) that are so characteristic of subacute bacterial endocarditis

STREPTOCOCCUS VIRIDANS SEPTICEMIA (SUBACUTE BACTERIAL ENDOCARDITIS?)—ATTEMPTED CURE BY EXCISION OF ARTERIOVENOUS ANEURYSM

Case 27 T B a negro laborer of 36 was admitted to the Philadelphia General Hospital on 9/9 38 complaining of pain in the joints chills and fever

HISTORY The patient was well until a month before admission when he developed a chill following considerable out of door exertion *This was followed the next day by joint pain and fever The fever continued until the time of admission to the hospital a month later During this time he lost 20 pounds in weight*

PAST MEDICAL HISTORY A lesion suggestive of chancre *was present 20 years prior to* admission There was a gunshot wound of the left thigh *nine years before admission*

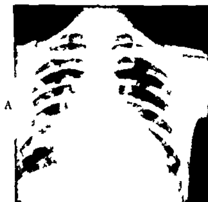
PHYSICAL EXAMINATION T 100 F B P 110/45 The area of cardiac dulness was increased in all diameters The apex beat was palpable in the fifth interspace *13 cm to the left of the midclavicular line No thrills were present The pulse was rapid* Corrigan in type and the rhythm was regular *There was a loud blowing systolic murmur heard over the entire precordium louder in the upright position* and a diastolic *murmur* was heard over the base of the heart The pulmonic second sound was accentuated The liver edge was firm and smooth and distinctly palpable under the right costal *margin* The spleen was palpable A thrill was felt over the femoral canal [illegible] cm below Poupart's ligament in an area *measuring* 16 sq cm On auscultation over the point of maximum intensity of the thrill a *deafening bruit was heard that could also be detected along the proximal vessels to the umbilicus and along the distal* vessels to the ankle Digital pressure over the point of greatest intensity caused both bruit and thrill to disappear Reflexes were normal except the patellar and Achilles on the left side which were absent Pulsations of the popliteal posterior tibial and dorsalis pedis were readily felt on the right but were barely palpable on the left side No varicosities or edema were noted in either thigh leg or foot No clubbing of the fingers or toes was present The skin temperature was the same on both sides The blood pressure in the right arm measured *1[illegible]0/[illegible]0 in the left arm 93/30, in the right leg 1[illegible]5/75 and in the left leg 85/50* The venous pressure varied from *115 mm to 1[illegible]5 mm*

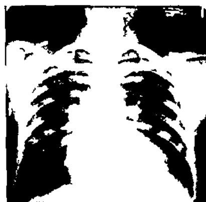
LABORATORY DATA A blood culture taken *on* the day of admission showed 1[illegible]0 colonies of *Streptococcus viridans* per cc of blood *A roentgen ray study of the heart showed enlargement in the transverse diameters There was hypertrophy of the left ventricle and some widening of the aorta* (Fig 88A) A film taken after compression of the arteriovenous aneurysm (Fig 88B) showed the heart to be slightly smaller and mottled density in the lung fields was not as marked as before compression An electrocardiogram was essentially negative Wassermann negative

CLINICAL DIAGNOSIS Arteriovenous aneurysm *Probable focus for S viridans* septicemia Cardiac hypertrophy with aortic regurgitation etiologic type unknown

a b

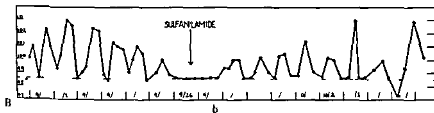
A



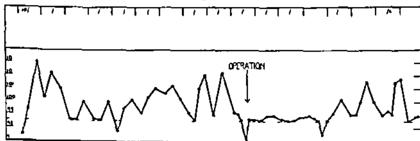


B

a




b




C

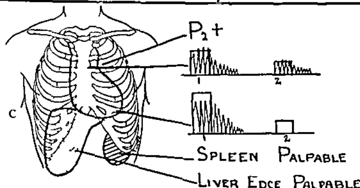


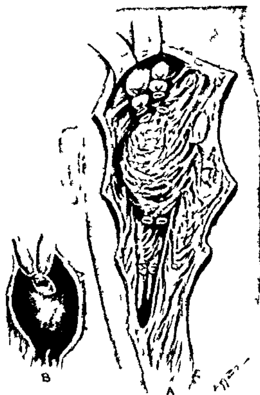

Fig. 88. A, Roentgenograms showing heart size (a) before compression and (b) after compression of the arteriovenous communication.
B, Temperature chart showing (a) effect of sulfanilamide therapy and (b) effect of operation.
C, Chart illustrating physical findings.

Discussion Following admission the fever persisted, and the anemia became more pronounced A second blood culture again showed *S viridans*, so it was evident that a focus was present and active Viewing the degree of cardiac damage it would appear that the blood stream infection, if primary in the aneurysmal varix had already reached the heart valves Continued observations however, failed to disclose any change in the character of the murmurs, consequently operation to remove the arterio venous aneurysm was considered If syphilitic heart disease were present with valves undamaged by the blood stream infection, removal of the infected varix offered the possibility of cure On the other hand if endo cardial involvement already existed the operation could do no harm and might benefit the patient to the extent of removing the strain of the arteriovenous aneurysm on the already damaged heart

The continued absence of embolic manifestations was a point against the involvement of the mitral or aortic valves or the endocardium of the left side of the heart Evidence of damage to the femoral artery and vein and of the re establishment of a subsequent fistula was sufficient to make us suspect that the point of origin of the septicemia might be in this area Sulfanilamide was tried from 9/21/38 to 9/26/38 (Fig 88B) and it succeeded in producing a transient fall in the temperature to normal and a temporary reduction in the number of *S viridans* colonies in the blood stream Since a marked increase in the degree of anemia was noted blood tranfusions were given When sulfanilamide was discontinued the temperature returned and the number of colonies per cc in the blood culture rose to the former level

After repeated trials, the status of the collateral circulation was found to be excellent consequently surgical removal of the arteriovenous aneurysm was decided upon A drawing (Fig 89) made at the time of the operation shows the dissection of the aneurysmal communication between the left femoral artery and vein in this patient After ligation the entire aneurysmal sac was removed Examination of the specimen showed on the arterial side of the communicating channel a ring of dark red friable vegetations No vegetations were present on the venous side of the orifice Microscopic examination of the sections using hematoxylin and eosin stain showed small clumps of dark blue cocci like bodies interpreted as being bacteria similar to the bacterial masses commonly seen on the heart valves in cases of subacute bacterial endocarditis

After operation the leg showed little change There was a slight decrease in the temperature of the operated side and a very slight swelling The patient s temperature (Fig 88B) promptly fell to normal following the operation The cardiac rate likewise dropped and clinical improvement was evident For nearly a week we were of the opinion that cure of the blood stream infection following the excision of the focus containing the vegetations had taken place However we were mistaken At the end of the first postoperative week the blood culture became positive and the temperature again began to show a gradual elevation On transfer back


A
B

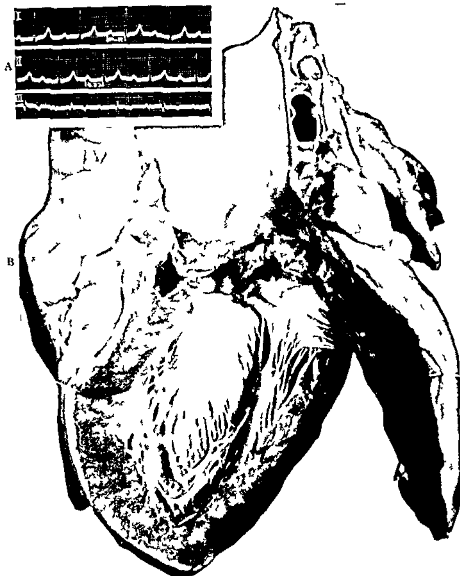



FIG 90 A The electrocardiogram Note prolongation of the P R Intervals to 0 3 second

B Subacute bacterial endocarditis superimposed upon calcific aortic stenosis The margins of the leaflets are fused thickened and calcified Note the extreme hypertrophy of the left ventricle and the smooth aortic wall above the valve (Autopsy No 27 911 *Philadelphia General Hospital*)

to the medical ward sulfapyridine was begun but the effect was the same as observed following sulfanilamide The temperature fell to normal, and the blood cultures were reported sterile from 11/16/38 to 11/30/38 On the latter date increasing dyspnea cyanosis and edema ushered in a rather sudden attack of congestive failure, and the patient died Autopsy was refused

Although we were unable to duplicate the success of Hamman and Rienhoff[146] and obtain a radical cure in this patient, we believe that if we had seen him earlier and had operated on him at once, the story might have had a different ending This case illustrates a type of heart disease rarely encountered where cure may be possible by excision of an infected arteriovenous communication

While we are discussing the value of operative procedures in subacute bacterial endocarditis attention must be called to the recommendation of splenectomy made by Riesman[316] When the spleen is large the patient's nutritional state good and congestive failure absent this operation imposes little additional risk The spleen is involved early in the course of the disease, consequently its role in feeding the blood stream may be an important one Viewed in this light its removal seems just as logical as the extirpation of the pelvic organs to prevent continual infections in gonococcal endocarditis or the removal of the arteriovenous aneurysm in the case just presented

The incidence of subacute bacterial endocarditis in patients with uncomplicated patent ductus arteriosus is high In Abbott's series of 92 cases death was caused by subacute bacterial endocarditis in 21 Graybiel Strieder and Boyer[140] were the first to propose surgical ligation of the ductus in these cases in an attempt to shut off the pathway to the blood stream They point out that the infection begins in relation to the pulmonary orifice of the ductus extending often to the pulmonary valves but rarely to the aorta Hence if an early diagnosis is made in cases of patent ductus arteriosus which is not impossible if they are constantly under observation surgical intervention must be considered Ligation has been successfully carried out by Gross (page 339) and seems justified in selected instances in an attempt to bar the bacteria and the vegetations from the blood stream in the hope that natural forces may be effective in healing the areas

## Calcific Aortic Stenosis—Superimposed Subacute Bacterial Endocarditis—Autopsy

**Case 28** W H a German cabinet maker of 49 was admitted to the Philadelphia General Hospital on 2/7/34 complaining of cough and dyspnea

History The patient was in fairly good health until two months before admission when he noticed chest pain that increased on exertion and radiated to the left arm Dyspnea was present A buzzing was felt in the chest when in bed at night Two weeks before admission edema of the ankles appeared for the first time this increased in severity until the day of admission

The patient denied venereal disease There was no past history of rheumatic infection

Physical Examination BP 110/90 T 101 F P 90 Petechiae present on the

conjunctivae The apex beat was in the sixth interspace 1 cm from the midsternal line A marked thrill was palpable over the second interspace to the right of the sternum A harsh systolic murmur was present over the same area transmitted to the vessels of the neck A systolic murmur was heard over the margin of the cardiac apex Rales were heard over both lung bases The liver edge was tender and palpable a hand s breadth below the right costal margin The spleen was not palpable No clubbing

LABORATORY DATA Blood culture negative Wassermann four plus Kahn negative R B C 3 200 000 W B C 5 600 hemoglobin 65 per cent (Sahli) P 76 L 4

Electrocardiogram prolongation of the P R intervals (First stage heart block) (Fig 90A)

Roentgenogram dilated aorta and cardiac enlargement (probably luetic)

CLINICAL DIAGNOSIS A Etiologic Rheumatic? Arteriosclerosis? Syphilis? B Anatomic Cardiac enlargement Aortic stenosis Relative mitral insufficiency C Physiologic First stage heart block Congestive cardiac failure D Functional Classification Class 4 Therapeutic Classification Class F

COURSE Congestive failure increased in spite of the usual therapeutic measures The blood cultures were negative although the patient had an irregular temperature for two weeks before death

AUTOPSY The heart weighed 660 Gm There was hypertrophy of the left ventricle The mitral valve was normal The aortic valve was entirely destroyed and replaced by calcium Superimposed upon this were firm masses of thrombi some of which showed calcification The end of a slate pencil could scarcely be pushed through the unopened aortic valve The aorta above the valve was smooth and conspicuously free of any pathologic change in contrast to the marked calcific lesion of the valve (Fig 90B)

DISCUSSION The aortic regurgitation and the positive Wassermann reaction in a man of 46 first suggested syphilis as the etiology However in the presence of the signs of subacute bacterial endocarditis the possibility that syphilis was the only etiologic factor diminished While bacterial endocarditis may be superimposed on syphilitic aortitis and valvulitis as the recent studies of Martin and Adams [8] indicate nevertheless it is a rare event The diagnosis should always be considered however in the presence of sepsis of undetermined origin a positive Wassermann reaction evidence of aortic insufficiency and a negative rheumatic history In this patient the harsh systolic murmur and thrill discovered over the aortic area in the absence of aneurysmal dilatation favor the diagnosis of a stenotic (rheumatic) lesion The calcific type of aortic stenosis has been discussed elsewhere (page 127)

The petechiae and the course of the fever in this patient were characteristic of subacute bacterial endocarditis even in the absence of a positive blood culture and also accounted for the positive Wassermann reaction This occurrence of biologic false positive Wassermann reactions in the presence of subacute bacterial endocarditis is not unusual Consequently it is not surprising that neoarsphenamine therapy has been suggested for these patients Stokes however opposes its use [7] Autopsy in this case proved the absence of syphilis and verified the correctness of this interpretation of the serology

The rapidity of the organization and calcification of the thrombi in this case in the absence of any treatment directed toward the process shows the natural tendency of the disease to heal

While the bacteriologist who isolates the *S viridans* from the blood stream *may refer to this organism as an invader of low virulence*, yet we are beaten as soon as he makes the diagnosis The mechanical features of the infection in most instances close the picture Masses of thrombi build up break off and are carried to vital centers by the blood stream In this patient it is hard to understand why the organism would pick out such a cardiac desert area as a totally calcified valve for implantation The valve it is true was the seat of previous damage but certainly in its calcified state it contained less blood supply than other lesions

The healing tendencies in this disease are evident in this desperate and almost successful attempt to organize and calcify the thrombi However the increase in the obstruction that this produced almost completely closed the valvular orifice and precipitated cardiac failure The absence of bacteria in many blood cultures is proof of the fact that the healing process was gaining the upper hand If in the future we can keep the blood stream sterile in subacute bacterial endocarditis and prevent large thrombotic masses from forming on the valve sites long enough for fibrous tissue to invade and organize the mass already present we may succeed in conquering this infection

# 6

# SYPHILITIC CARDIOVASCULAR DISEASE

The same medicine will both harm and cure me—Ovid *Tristia* Bk ii 1 20

The incidence of cardiovascular syphilis in any country today is an index of the intelligence of its population in general and of the ability and foresight of its medical profession in particular While rheumatic infection remains one of the grave problems of modern civilization syphilitic heart disease can be greatly minimized by the recognition and adequate treatment of early lues Considering the high mortality rate among patients with advanced cardiovascular syphilis it is small wonder that a nation wide intensive campaign was launched recently to educate the public and bring the early cases under competent medical supervision The careless attitude of the average private physician in regard to the treatment of syphilis has been responsible for organized efforts on the part of the governments of many countries to combat the disease Since a full understanding of the anatomic and pathologic aspects of syphilitic involvement of the heart and great vessels is a necessary prelude to intelligent management a brief review of these fundamental principles will precede the discussion of therapy

## THE LESION

**Chancre** The primary lesion of syphilis is the chancre Accumulative evidence points to the fact that the blood stream is invaded by the *Treponema pallidum* before the appearance of this primary lesion It may be possible in many cases that the spirochete has already reached the aorta before clinical manifestations of syphilitic infection are noted When a chancre is in evidence local medical or surgical measures directed toward the initial lesion are of no avail since both blood stream and lymphatic system have transported the spirochete far beyond the reach of regional medication Many spirochetes invade nearby lymph nodes and are killed by the resistance forces of the body Others penetrate deep into the lymphatic channels finally reaching the thoracic duct and the venous blood stream During the initial shower of spirochetes many penetrate as far as the lymph nodes in the thorax and from here by lymph movement reach the vasa vasorum in the aorta

**Obliterative Endarteritis** In these small vessels within the artery wall an initial obliterative endarteritis develops which may slowly spread

to the whole ascending portion of the aorta The seriousness of this destructive process can readily be realized when we recall that the cusps of the aortic valve are attached in this area When this section of the aorta becomes the seat of scar formation the valve is drawn backward and regurgitation develops It is important to note that the damage takes place without stenosis which distinguishes it from the rheumatic type in which adhesions develop between neighboring cusps, obstructing the flow of blood and at the same time interfering with valvular function

**Aneurysm** If the spirochetal invasion in the aortic wall is unchecked it plays havoc with the muscular media Degeneration of this coat is reflected in the pallor and wrinkling of the intima The whole aortic wall becomes weakened by the destruction of this vital tissue, eventually dilates and saccular aneurysms result If the process of dilatation widens the aortic valve and causes regurgitation the heart will be affected, with the development of cardiac hypertrophy However if regurgitation does not occur and the coronary ostia escape an aneurysm of the aorta usually has no effect on cardiac size or function It can, of course cause symptoms by pressure on any of the surrounding structures depending on the part of the arch involved and the direction in which the sacculation points For example the aneurysm may press on the trachea and bronchi with the appearance of the typical brassy cough Adhesions to the trachea may give rise to a tracheal tug (Oliver s sign) while compression of a bronchus if long continued will result in atelectasis If the aneurysm points posteriorly it may erode the vertebrae and cause severe pain The erosion on the other hand, may be in an anterior direction in which event a pulsating tumor will appear on the anterior chest wall (Fig 91) Aphonia appears when the recurrent laryngeal nerve is involved in the process Many times if aneurysms do not press on the structures above mentioned and do not cause erosion they may reach a large size without attracting attention

If aortic dilatation is moderate and regurgitation develops the pressure on the weakened arch is relieved and no aneurysm appears However the situation is still far from a happy one since cardiac hypertrophy occurs and the patient will eventually succumb to congestive failure

**The mouths of the coronary arteries** are situated in a bad neighbor hood as far as the syphilitic patient is concerned, and may be invaded early in the disease in which event serious symptoms occur Angina appears and with it the likelihood of sudden death at any time Willius[406, 410] has shown that the coronary arteries occasionally rise above the level of the sinuses of Valsalva and in this location they stand a much greater chance of involvement in a syphilitic process than when they take their origin from the aorta at a lower level The effect of a syphilitic involvement of the coronaries differs in no way as far as the patient s symptoms are concerned from an arteriosclerotic process An anoxemia is produced in the heart muscle and this is attended by pain In syphilis the coronary arteries are generally free of involvement along their course which may

account for the infrequency of thrombosis Coronary occlusions following arteriosclerotic heart disease are more common during the winter months while those that complicate syphilitic aortitis show no seasonal variation Pean and Mills [3] believe this is a result of the steady progression of the syphilitic lesion

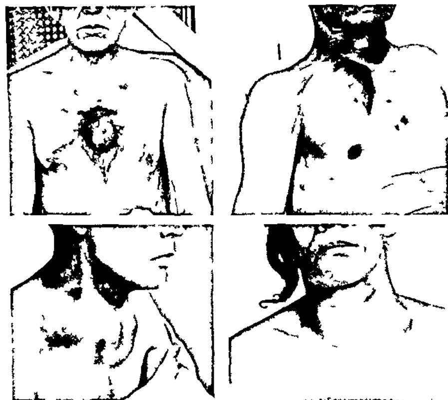


Fig 91 Aneurysms of the aorta S ellings of this type are at times confused with other tumors of the chest wall

The heart itself is seldom invaded by the spirochete If secondary changes are discovered in the heart muscle in syphilis they are usually produced by the narrowing of the coronary mouths in the aorta or result from a complicating arteriosclerosis Gummas of the heart producing heart block or other symptoms, are rare Von Haam and Ogden[143] collected reports of only seven cases from the literature between 1845 and 1935 In a study of 5213 autopsies of their own they reported gummatous lesions of the heart in only three instances

From this description it is evident that the earlier the cardiac invasion is detected the better will be the result of specific therapy However this

cannot be accomplished unless we suspect the presence of the infection The constantly alert physician will report a much higher incidence of cardiovascular syphilis in his practice because his suspicions are aroused by small details in the history and physical examination If instead of dismissing these small departures from normal he follows them with determination until positive proof is obtained either by further study from a confession from the laboratory or by a consultation cardiovascular complications of middle life may be largely prevented The student makes the mistake of regarding the aneurysm or the cor bovinum resulting from aortic regurgitation seen at autopsy as typical evidence of cardiovascular syphilis He returns to the wards to seek them clinically and later in his practice as a result of a lack of knowledge fails to recognize the earlier manifestations

## SIGNS

*At this point the question properly arises What are the early signs of* cardiovascular syphilis? The different criteria in use in various clinics and the lack of uniformity of opinion even among experts in the matter serve to confuse the practitioner We must acknowledge at the start that this diagnosis is most difficult and the criteria are far from settled However the careful physician should not be discouraged for here is a clinical problem that should challenge his skill and arouse his interest

**Aortic Second Sound** Unless the syphilitic process involves the coronary mouths and causes aortic regurgitation or weakening of the aortic wall its presence is apt to elude the physician who does not always keep the possibility in mind Certainly the scars in the first part of the aorta which the pathologist so triumphantly points to at autopsy can furnish him no clue at the bedside The higher up in the arch these scars are situated the greater will be the clinical silence they maintain However something can still be said concerning the character of the aortic second sound that accompanies this structural alteration Its tambour or drum like quality in the presence of syphilis may reflect a tissue change progressing in the aorta as a whole If we keep in mind the fact that hypertension or arteriosclerosis produce structural alterations, and consequently a similar change in the tone of the aortic second sound a tambour quality of the aortic second sound should serve to sharpen our suspicion It is not in itself diagnostic

**The systolic aortic murmur** that may be heard at the time of early syphilitic invasion is a less certain sign It too may accompany arteriosclerosis but at the same time it can also serve as a building stone in our diagnosis of early syphilitic aortitis

**Fluoroscopic Examination** If the patient who has these indefinite signs on physical examination is examined fluoroscopically suspicion may be strengthened The aorta in early syphilis is slightly wider and more dense than normal (page 43) and in addition there may be noted a

slightly increased pulsation These changes in my opinion are most suggestive and valuable when reported by an observer who has had considerable experience with the fluoroscopic method Even then they do not establish the diagnosis beyond doubt but only forge another link of similar strength in the chain of evidence

**Other systems of the body** may contribute more clear cut evidence of syphilis if the physical examination is carried beyond the region of the heart For example the presence of signs of neurosyphilis should be sought since this form of involvement often co exists in the same patient In the Co-operative Clinical Studies in 191 cases of uncomplicated syphilitic aortitis in which lumbar punctures were made within a month of the detection of aortitis 49 per cent showed unquestionable spinal fluid abnormalities Consequently a spinal fluid examination is an indispensable part of the examination of every patient who has cardiovascular syphilis

**Unequal Simultaneous Blood Pressure** Herzog[16] states that the diagnosis of syphilitic aortitis should be suspected when the blood pressures taken in both arms simultaneously are shown to be unequal To accomplish this two blood pressure cuffs are needed These are connected to the manometer by means of a Y tube The use of a symballophone enables the observer to detect the exact time of the appearance of the pulse beats in each arm

We cannot depend on any abnormalities of the electrocardiogram to diagnose syphilis Heart block occurs in association with sclerotic or coronary disease but is rarely caused by syphilis Auricular fibrillation is very rarely present as a complication of syphilitic aortitis a fact that may be valuable at times in ruling out syphilis in doubtful cases

## SYMPTOMS

The symptoms that are encountered in syphilitic aortitis are few and these are by no means characteristic The fact that they sometimes tend to be sudden in onset however should arouse suspicion The abrupt appearance of the signs of circulatory failure dyspnea cough edema substernal pain particularly in young patients may be significant The dyspnea may remain as a nocturnal occurrence while other signs of failure may progress These however are late manifestations and usually come on at a time when treatment offers less permanent benefit

Reports from the various clinics show that serologic tests in patients with cardiovascular syphilis are positive in 75 to 80 per cent of the cases[63] [4] [6] This figure however is much less when previous although inadequate treatment has been given[76] Consequently while a negative Wassermann test does not rule out syphilis (page 56) its routine use will serve to bring under scrutiny a larger group of patients before damage is evident in the cardiovascular system at a stage when properly direct treatment may prevent its development

## PROBLEM OF EARLY DIAGNOSIS

In the light of this review, it is evident that the detection of cardiovascular syphilis is quite easy if it is advanced, but difficult if not impossible *in its earlier stages*. The earlier the diagnosis, the greater will be the success of the treatment from the cardiovascular standpoint. No clue that can be obtained from a complete history, a thorough physical examination including neurologic survey and laboratory study (roentgen ray fluoroscopy electrocardiogram serologic tests of blood, and a complete spinal fluid examination including cell count globulin estimation, colloidal curve and quantitative Wassermann test) should be omitted. Cardiovascular syphilis should then be diagnosed in from 5 to 25 per cent of the cases of heart disease in the practice of the average physician, depending of course on his location. If his figures are less than the minimum stated above, he is probably missing the diagnosis in some instances.

Welty[398] has recently analyzed the incidence of cardiovascular syphilis in the records of 15 000 consecutive autopsies at the Philadelphia General Hospital. In 1 040 cases (6 93 per cent) cardiovascular syphilis was diagnosed. Aneurysm was present in 192 patients aortic insufficiency in 216 and simple aortitis was found in the remaining number.[63] Males predominated in this series (74 per cent) while 68 per cent were negroes. When *these cases are divided into five groups of 300 autopsies each a decreasing* incidence of cardiovascular syphilis is seen (Table VI).

TABLE VI

DECREASING INCIDENCE OF CARDIOVASCULAR SYPHILIS AT THE PHILADELPHIA GENERAL HOSPITAL (After Welty)

| Years | Number of Cases | Incidence | Ratio |
|---|---|---|---|
| 1927 to 1930 | 276 | 92 per 1000 | 1 per 11 deaths |
| 1930 to 1932 | 231 | 77 per 1000 | 1 per 13 deaths |
| 1932 to 1934 | 191 | 63 6 per 1000 | 1 per 16 deaths |
| 1934 to 1935 | 174 | 58 per 1000 | 1 per 17 deaths |
| 1935 to 1937 | 168 | 56 per 1000 | 1 per 18 deaths |

## TREATMENT

### SPECIFIC THERAPY

During recent years many problems in the treatment of cardiovascular syphilis have been solved. We can now formulate a scheme of therapy for each case upon much more firm ground than was formerly possible, when it was the prevailing custom to recommend the same program of treatment for all syphilitic patients. The less specialized therapy of yesterday was attended by numerous accidents among the cardiac patients of the group who had early aortic involvement. Vigorous treatment with arsenicals was

followed by sudden death in many cases while it produced in others a rapid onset of the symptoms of heart failure This led the medical pendulum to swing away from the use of the arsenicals in cardiac patients Today we are in the mid position and are again employing arsenicals in cases of uncomplicated syphilitic aortitis, but we have learned to be cautious and precede their use by adequate preparation with slower acting and safer drugs

The early accidents following the injection of arsenicals were due many times to therapeutic shock (Herxheimer reaction) caused by too sudden destruction of large numbers of spirochetes and the liberation of their endotoxins This was invariably attended by a sudden swelling or reaction in the aorta about the mouths of the coronary arteries Moore [74] believes that the Herxheimer reaction may cause a coronary occlusion a rupture of an aneurysm or if there is cerebral vascular involvement the sudden edema and infiltration may cause a cerebral hemorrhage In other cases the arsphenamine may prove too toxic for the already damaged heart muscle and cause ventricular tachycardia and fibrillation Vigorous approach with arsenicals in other cases may be followed by immediate clinical improvement but after this by a rapid downhill course (therapeutic paradox) caused by the scar tissue replacement in the luetic areas

A safe procedure to prevent these reactions is to begin treatment of the patient who has syphilitic aortitis with a heavy metal and iodide Bismuth is the heavy metal of choice First introduced in 1921 by Sazerac and Levaditi bismuth has succeeded in completely replacing mercury in the treatment of cardiovascular syphilis When given by intramuscular injection this heavy metal is slowly absorbed and excreted and a low but uniform concentration is maintained in the tissues As long as the bismuth is present the multiplication of the spirochetes is prevented although they are not destroyed This fact can be proved by animal experimentation While the exact mechanism of this action of bismuth on the spirochete is unknown the effect is not the same as that exerted by the arsenicals In the sense that it prevents multiplication of spirochetes in the syphilitic lesions thus allowing the defense mechanisms of the body aided by the iodides to heal the lesions bismuth may possess resistance building properties

The necessary concentration of bismuth can be maintained in the body by weekly intramuscular injections of one of the preparations of the insoluble salts The soluble salts are painful more toxic and require more frequent administration Consequently they are more expensive and less convenient for the patient I prefer bismuth salicylate a ten per cent suspension in oil The dose is 0 2 Gm (2 cc ) once weekly This preparation causes very little local discomfort and toxic reactions following its use are rare

Intramuscular injections of bismuth preparations are best given into the inner angle of the upper outer quadrant of the buttock (Fig 92) using a 2 to 2½ inch (21 gauge) needle on a 2-cc syringe The drug is

introduced deep into the body of the muscle Since an insoluble preparation is being used an aspiration test is essential before the injection is made to detect a chance entry into a deep blood vessel Following the *injection the site should be massaged for a minute to favor distribution*

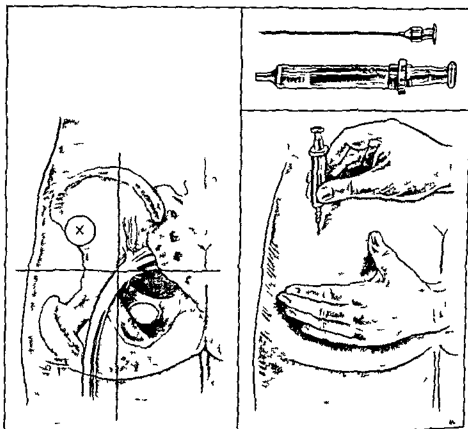


Fig 9 Equipment and technic for intramuscular injections
A cc syringe (21 gauge) ½ inch needle
B Site of injection inner angle of upper outer quadrant
C Technic of injection

and better absorption of the drug Sterile abscesses following bismuth salicylate in oil are infrequent

Early in the course of bismuth therapy a *bluish gray line may appear* at the gum margins Less often a stomatitis appears, particularly in patients whose oral hygiene is poor Few alterations in renal function have been observed following a course of bismuth in the usual dosage and clinical evidences of liver damage are rare Aching of the bones and muscles quite like that produced by grippy or influenzal infections is often complained of during bismuth therapy, but its cause so far is unknown *Seldom do*

Herxheimer reactions occur when bismuth is used in the treatment of cardiovascular syphilis On the whole the toxic effects produced by bismuth compared to those observed following mercury and arsenicals are few

Intramuscular injections of bismuth iodide therapy and later the cautious use of intravenous injections of neoarsphenamine comprise the usual procedures of treatment in cardiovascular syphilis Lately a preparation of bismuth for oral administration has appeared on the market This semisolid termed sobisminol mass, is a complex organic bismuth product the exact chemical nature of which has not been fully established[33] It is obtained by the interaction of sodium bismuthate tri isopropanolamine and propylene glycol and contains between 19 25 and 20 25 per cent of bismuth The recommended adult dose consists of two to three capsules each representing 150 mg of metallic bismuth taken with plenty of water at 10 A M 3 P M and 8 P M When continued in this dosage for from 10 to 12 weeks they represent a course of bismuth therapy For children the dose is one capsule three times a day Such oral administration has been shown to produce a blood concentration of bismuth comparable to that following intramuscular injections Satisfactory antisyphilitic concentrations of bismuth are also found in the urine and cerebrospinal fluid[67]

Sobisminol mass given orally may produce gastro-intestinal upsets in some patients occasionally severe enough to cause them to discontinue the drug This is a disadvantage Bismuth stomatitis may appear and a bismuth line has been noted in some instances When the treatment is placed in the hands of the patient dosage is less accurate and there remains the tendency on the part of the patient to neglect to take the medicine as soon as improvement occurs Furthermore the physician is not apt to have as frequent contact with his patient and this gives less opportunity to observe either the untoward effect of the drug or the progress of the cardiac lesion No sustained bismuth effect is derived from the use of sobisminol by mouth since the excretion of bismuth in the urine falls off rapidly as soon as the capsules are discontinued Relapses therefore occur more readily since no bismuth depot is established when the oral route is used When intramuscular injections are used the full amount of the drug is administered

Occasionally some patients for business or professional reasons find it impossible to report to the physician at weekly intervals Likewise in rare instances intramuscular injections have to be discontinued because of pain and induration in the muscles In these cases the temporary oral administration of bismuth is useful

If oral bismuth therapy gains headway in the future the distribution of preparations of the drug should be carefully controlled Oral administration should remain under the physician s supervision since self medication in cardiovascular syphilis is extremely dangerous

The use of iodides in the treatment of cardiovascular syphilis is based upon the local healing effect of these drugs If given alone at any stage of the disease they have little influence on the spirochete When combined

with a heavy metal or an arsenical symptoms are more speedily controlled and the local healing produced by the iodide allows the more powerful antisyphilitic drugs to penetrate deeply into the tissues A similar effect on necrotic tissue is seen when iodides are used in other granulomatous dis eases especially actinomycosis

When administered by mouth the absorption of the iodides is rapid Either the potassium or the sodium salt may be used although the latter is more expensive It is best to prescribe iodides in concentrated solution

| | |
|---|---|
| KI | 50 0 Gm |
| Water | 50 0 cc |

In this prescription one drop will contain approximately 0 065 Gm (1 grain) of KI The required dose should be dropped into a full glass of water or milk and given just before meals The usual dose of the above prescription is 2 to 4 Gm (30 to 60 grains) three times a day Iodides should be administered for periods of three months twice a year in com bination with the heavy metal and not with neoarsphenamine When tuberculosis or simple goiter complicate the picture the administration of iodides is contraindicated

Some patients show an intolerance to iodides Coryza and an unpleasant brassy taste in the mouth may be disregarded However if gastro-intestinal irritability develops or severe acneiform eruptions appear, the drug should be at least temporarily discontinued In some instances the healing action of the iodides on syphilitic tissue with subsequent absorption of necrotic products may produce fever which subsides when the drug is withdrawn

After the preliminary course of 12 weeks of bismuth and iodide neo-arsphenamine may be started cautiously Doses of 0 1 Gm (intravenously) should be administered at first and the amount gradually increased until 0 45 Gm is given at the fifth dose of a ten injection series[67-91] Ars phenamine should never be used in cardiovascular syphilis

Many variations are possible in the therapeutic schedule in this type of syphilitic involvement It is difficult to recommend a schedule that will fit every case Experience will soon show that each individual presents certain rules of his own and the most successful result is achieved by the physician who learns to follow them The age and build of the patient the duration of the infection the amount of previous treatment and the social status are all factors of importance that must be considered In short, in order to get the best result the physician must be skilled in the art of medicine and be able to interpret the symptoms of the patient in terms of the structural changes He should also be quick to detect any reactions that call for a pause in therapeutic activity

If congestive failure is present when the patient is first seen the usual measures described in Chapter 2 are carried out Digitalis should be given to the point of digitalization and then continued in a maintenance amount The organic mercurial diuretics are useful Many of these patients

are unfit for heavy metals when first seen but if edema clears and balance is restored bismuth and potassium iodide may be started

If aortic regurgitation is present and congestive manifestations have not appeared after the 12 weeks of preparatory treatment using bismuth and iodide neoarsphenamine may be cautiously started using an initial dose of 0 1 Gm and increasing this dose gradually depending on the body weight until a maximum of 0 45 Gm is reached in 12 treatments at weekly intervals It is most important to avoid reactions of all types with this course of treatment If reactions occur arsenicals should be discontinued and after a short rest period intramuscular injections of bismuth should be given If no reactions are encountered and the course of arsenicals is completed heavy metal and iodide for 12 weekly doses are again indicated In the absence of untoward symptoms these courses may be given alternately over a period of two years In each case the cardiac lesion is the guide to treatment and frequent examinations of the heart should be made

When angina is present and syphilitic involvement of the coronary arteries is suspected the prognosis is grave It is well to send these patients to the hospital if possible Bed rest and potassium iodide supplemented by the usual measures directed toward the relief of the angina are called for (Chapter 7) If improvement occurs heavy metal may be added I have never used arsenicals in this group of cases

In the presence of aneurysms great care should be taken to guard against reactions Heavy metals preferably bismuth should initiate the treatment and should be continued with iodides for ten weeks If arsenical therapy is used start with exceptionally small doses (0 025 or 0 05 Gm) and increase slowly to 0 2 Gm in a 12 dose series These patients should be examined frequently and carefully (see Case 98)

As stated in the recent summary of the Co operative Clinic Group[68 69] the best treatment is prophylaxis At least 30 injections of an arsenical and 60 injections of interim heavy metal (bismuth) administered under the continuous system while the patient is in the early stages of syphilis is after all the best form of therapy for the prevention of cardiovascular involvement This has been shown by Thompson and his co workers in a survey of 260 individuals who contracted syphilis 15 to 25 years before the study was made The incidence of cardiovascular involvement in the group was found to be 10 per cent a figure that agrees with the observations of other investigators However in the group studied by Thompson Comeau and White[374] all of the cases showing evidence of cardiovascular syphilis gave a history of inadequate early treatment

With treatment carefully planned and carried out a marked symptomatic relief is possible in patients suffering from syphilitic invasion of the cardiovascular system Proper therapy increases the average duration of life in the presence of uncomplicated syphilitic aortitis from 34 to 85 months[68] The average duration of life in patients who are treated with

small doses of arsenicals exceeds the duration of life of patients who are treated with large doses

### Treatment of Aneurysms

WIRING CAROTID-JUGULAR ANASTOMOSIS

(See page 229)

## ILLUSTRATIVE CASES

### Untreated Syphilitic Cardiovascular Disease—Aortitis, Aortic Regurgitation and Cardiac Enlargement—Death Following First Attack of Congestive Failure—Autopsy

*Case 29* J M a colored laborer of 43 was admitted to the Philadelphia General Hospital /7/31 complaining of shortness of breath swelling of the legs and pain in the chest

History The dyspnea appeared a year before admission and gradually progressed to orthopnea A month before admission precordial pain was noticed It was referred to the left shoulder and appeared on slight exertion Edema of the feet in the evening came on six weeks before admission this increased rapidly and was generalized when the patient entered the hospital

Past History Chancre at the age of 18 No treatment

Physical Examination Cyanosis orthopnea anasarca B P 170/0 pulse 130 regular and Corrigan in type The heart was enlarged to the left (L B 16 0 cm) There was a diastolic murmur over the aortic area and absence of breath sounds accompanied by a flat percussion note over the right lower chest below the scapular angle (Fig 93A)

Laboratory Data Blood count normal Wassermann reaction positive The urine showed a cloud of albumin with hyaline casts

The roentgenogram showed generalized cardiac enlargement a wide aorta and fluid at the right base

The electrocardiogram showed a left axis deviation inverted T1 low voltage *QRS* and slightly prolonged P R intervals

Clinical Diagnosis A Etiologic Syphilis B Anatomic Cardiac enlargement Aortic regurgitation Aortitis involving the coronary ostia C Physiologic Normal sinus rhythm Anginal syndrome Congestive cardiac failure D Functional Classification Class 4 Therapeutic Classification Class E

Course The patient died suddenly on the fourteenth hospital day

Autopsy (Fig 93B) There was considerable cardiac hypertrophy The aortic valve leaflets were bound down to the aorta by syphilitic scar tissue The thoracic aorta was dilated and the seat of striations typically luetic The coronary orifices were stenosed but the coronary arteries themselves were normal throughout their course

Discussion On admission this patient presented all the signs and symptoms of advanced congestive failure The search for the etiologic background was a short one An initial lesion at the age of 18 with no subsequent treatment the negative rheumatic history the race, the age the evidence pointing to aortic regurgitation as the single lesion and the positive Wassermann reaction made the diagnosis of syphilitic cardiovascular disease inescapable

The usual rapid progress in the heart failure is evident Symptoms first appeared six weeks before death The anginal pain complained of on slight exertion suggests involvement of the coronary ostia in the syphilitic process

A

Pulsating Carotids

Dull Area (Dilated Aorta)

$P_2$ +

1 2

1 2

Area of Flatness and Distant Breath Sounds

B

Fig 93 Syphilitic cardiovascular disease Syphilitic aortitis Note aortic dilatation and marked cardiac hypertrophy (Autopsy No 839 Philadelphia General Hospital)

consequently the blood supply to the myocardium must be limited This may have been an important factor in the rapid downhill course and may explain the failure of the usual therapeutic measures to restore compensation

The history of the untreated primary lesion at the age of 18, and the long period of apparent latency of the infection (25 years) followed by rapidly developing signs of cardiac failure at the age of 43 are not uncommon Syphilitic involvement of the heart and aorta can exist in the absence of symptoms for many years as this man's story illustrates The development of aortic regurgitation paved the way for the cardiac failure and the coronary involvement hastened the end The patient, during the development of the disease, had no occasion to seek medical advice He felt well and continued to work as a laborer When symptoms finally developed at the age of 42, they succeeded one another rapidly

When cardiac failure appeared and the patient was admitted to the hospital the heart and not the syphilis demanded attention The measures employed in these cases are the same as in any case of congestive failure (Chapter 2) Angina should also be treated in the usual manner (Chapter 7) If severe anginal pain is present and is unrelieved by ordinary medical measures alcoholic injections are to be considered (page 256)

### Rheumatic Heart Disease Mistaken for Syphilitic Aortitis in Presence of Positive Wassermann Reaction—Autopsy

**Case 30** C B an Italian shoemaker of 50 entered the Philadelphia General Hospital on 5/13/34 complaining of chest pain and increasing shortness of breath

History Dyspnea was present for some years but became worse the month before admission and was soon followed by edema Chest pain on exertion was noted three weeks before admission

Past History Negative for syphilis Positive for rheumatism at age 5

Physical Examination B P 180/30 Orthopnea Edema of legs Rales at both lung bases Apex of the heart in the sixth interspace 15 cm to the left of the midsternal line Rhythm irregular Rate 100 Heart sounds were of poor quality Harsh systolic and diastolic murmurs were heard over the aortic area There was a long low pitched diastolic murmur over the mitral area

*Laboratory Data Blood Wassermann positive Urine showed* a cloud of albumin with many hyaline casts

The electrocardiogram showed many ventricular premature beats and a left axis auricular fibrillation

The patient d ed on the fifth hospital day

Clinical Diagnosis A Etiologic Syphilis B Anatomic Cardiac enlargement Aortic regurgitation C Physiologic Numerous premature ventricular contractions D Functional Classification Class 4 Therapeutic Classification Class E

Autopsy Both ventricles were dilated and hypertrophied The aortic and mitral valves showed the presence of an old rheumatic endocarditis The aorta showed very few healed syphilitic scars

**Discussion** In addition to the signs of congestive cardiac failure in this patient there was evidence of heart disease of long standing cardiac enlargement and the murmurs over the apex and the aortic area A Corrigan

type of pulse was present and the patient was found to have a positive Wassermann reaction Over the region of the cardiac apex there was a low pitched rumbling diastolic murmur This did not excite suspicion and was considered to be an Austin Flint murmur Consequently the etiologic background was thought to be syphilis Response to treatment was poor which seemed to confirm the diagnosis and the patient died on the fifth hospital day




Fig 94 Rheumatic involvement of the aortic valve Healed syphilitic aortitis (Autopsy No 7596 Philadelphia General Hospital)

The main lesion found in this man's heart at autopsy was rheumatic (Fig 94) although the pathologist found some slight evidence of syphilitic aortitis

Reviewing this case in the light of the autopsy findings we must realize that at times it may be impossible to ascertain the exact etiology of a cardiac lesion After all the clues offered by clinical and laboratory studies

*are fully investigated, considerable doubt may still exist* Aortic valve lesions when they occur alone cause most confusion (page 204) However, the systolic and diastolic murmurs over the aortic area the typical rumbling diastolic murmur at the apex the positive rheumatic history and the duration of the dyspnea should make us consider rheumatic heart disease The positive Wassermann the aortic lesion and the sudden death of the patient during the first episode of congestive failure suggested syphilis as the background before the autopsy

Calcific aortic stenosis should also have been considered in this case Evidence of calcification of the aortic valve on the roentgenogram (see *Fig 26) would have strengthened a rheumatic diagnosis The presence of* the systolic murmur over the aortic area if accompanied by a thrill is usually evidence in favor of rheumatic etiology although occasionally *aneurysmal dilatations may produce a thrill in this area*

*In this patient evidence of syphilis in other parts of the body wa* entirely lacking in fact the Wassermann reaction alone seemed to sway clinical opinion toward syphilis

The electrocardiogram was returned to us after the autopsy In keeping with our impression of syphilitic heart disease we believed the irregular rhythm was due to frequently recurring premature beats However *the tracing showed the presence of auricular fibrillation an arrhythmia* much more likely to complicate the course of rheumatic heart disease than luetic

Occasionally cases in which an etiologic diagnosis of the aortic lesion cannot be made develop fever and other evidences of subacute bacterial endocarditis However while pointing to a rheumatic background in most cases, this complication is possible in congenital luetic or rheumatic types in fact it should always be kept in mind when discussing the cause of death of any cardiac patient Maher and Plece [5] have reported 12 instances from a series of 5000 cases in which syphilitic heart disease was complicated by the appearance of thyrotoxicosis This added burden increases the incidence of auricular fibrillation and congestive failure Successful surgical treatment of the thyrotoxicosis is usually followed by considerable clinical *improvement The mortality following subtotal thyroidectomy was sur* prisingly low in the series observed by Maher and Plece

*A final point of importance in arriving at the correct etiologic diagnosis so essential before proper treatment can be begun is the possibility of* rheumatic and syphilitic infections co existing in the same heart *Cases of* this type illustrated by the patient now under discussion are by no means rare

The treatment of this patient was first directed toward the cardiac failure If this had cleared the importance of establishing the correct etiologic background for the heart lesion at once becomes evident The treatment of the syphilis would then have proceeded cautiously with the cardiovascular system *in mind followed by frequent examinations to* ascertain the effect on the cardiac lesion

### Syphilitic Aortic Aneurysm of Transverse Arch (Aneurysm of Symptoms)—Steady Down Hill Course with Cough and Dysphagia—Autopsy

**Case 31** R A., an unemployed colored male of 53 was admitted to the Philadelphia General Hospital on 5/ 0/ 9 complaining of pain in the chest and shortness of breath



Fig 95 Large aneurysmal sac a ising from ascend ng aort c arch Not th small size of the heart compared to that of the aneury n (Autopsy No 0 8 0 Philadel ph a General Ho pital )

History Chronic cough for six years Increa ng hoarseness and dyspnea followed by dysphagia and a lo s of weight of 40 pound appeared du ing the y a before admission

PHYSICAL EXAMINATION Marked dyspnea B P 110/80 on the right and 0/0 on the left Limited expansion of the left side of the chest Fullness over the left upper chest The breath sounds were distant over this area and exaggerated over the right chest There were rales at both lung bases There was a systolic murmur over the cardiac apex No cardiac enlargement A2 greater than P2

LABORATORY DATA Wassermann positive The roentgenogram showed a large aortic aneurysm The trachea was displaced to the right

Electrocardiogram normal

Urine showed a trace of albumin

CLINICAL DIAGNOSIS A Etiologic Syphilis B Anatomic Large aortic aneurysm C Physiologic Normal sinus rhythm D Functional Classification Class 4

The patient died suddenly on the 12th hospital day

AUTOPSY The heart was small compared to the size of the aneurysmal sac (Fig 95) About one inch above the aortic valve the aorta was seen to expand into a large aneurysmal sac measuring 15 × 16 × 10 cm and involving the remainder of the ascending and all of the transverse arches The sac was filled with thrombus and was attached to the apex of the left lung which was pushed forward and compressed There was likewise compression and erosion of the esophagus with a large ulcer The pulmonary artery where it divides and passes into the lungs showed constriction resulting from the aneurysm

DISCUSSION The complaints of dyspnea cough and dysphagia focused attention at once on the mediastinum in this case and suggested aneurysm The clinical examination and the roentgen study quickly confirmed the diagnosis

Patients with aneurysm in this location lose considerable weight (aneurysmal cachexia) This may be a result of the continued pain which causes a loss of sleep In the case under discussion the dysphagia appeared to be an additional and perhaps a more direct cause of the weight loss Compression of the lung and trachea with atelectasis contributed to the dyspnea at the same time producing cough and hoarseness

The autopsy showed nothing to explain the patient s sudden death However some notice must be taken of the fact that the pulmonary artery was markedly compressed by the aneurysmal sac Encroachment in this area if long continued can in itself lead to cardiac failure through the production of cor pulmonale (page 426) Had this patient survived for a longer period clinical evidence of this pressure in the lesser circulation would have appeared in the form of cyanosis engorged pulsating jugulars, increasing dyspnea enlarged liver and the signs that we interpret as evidence of right sided heart failure Occasionally the dilated aorta may rupture into the pulmonary artery with the production of an arteriovenous aneurysm A loud prolonged murmur accompanied by a thrill then appears over the pulmonary area dyspnea increases and hemoptysis may occur This accident does not cause immediate death in fact, as we have seen in Case 6 the patient may live long enough to develop secondary changes in the wall of the pulmonary artery

The patient under discussion received a liquid diet and sedatives in sufficient quantities to relieve the cough and dyspnea The heart was not enlarged and aside from the dyspnea and slight cyanosis which could not

be considered entirely cardiac in origin there were no signs of cardiac failure Digitalis was not prescribed

Bismuth salicylate injections (page 214) and iodides by mouth were given for the effect they might have in reducing the pain by their specific action but were unsuccessful

SYPHILITIC AORTITIS AND ANEURYSM—EXCELLENT RESPONSE TO THERAPY*

**Case 32** E H a well nourished white woman of 51 consulted her physician in January 19 9 because of severe pain in the left shoulder chest and upper arm Her husband d ed a month previously of a ruptured aortic aneurysm

PHYSICAL EXAMINATION BP 14 /90 There was an increase in the area of supra cardiac dulness noted and a marked accentuation of the aortic second sound

PAST HISTORY Her blood Wassermann was positive in 1919 at hich t me appro priate therapy as begun but discontinued because of a reaction the exact nature of which was not clear No treatment was received between 1919 and 19 9

The roentgen examination (1929) (Fig 96A) showed d latation and increase in expansile pulsation of the first portion of the arch of the aorta The greatest width of the aortic shadow was 8 5 cm

CLINICAL DIAGNOSIS A Etiologi Syph l s B Anatomic Ao titis Early aneurysm of the ascend ng arch C Physiolo c Normal sinus rhythm D Funct onal Classificat on Class

SUBSEQUENT COURSE Weekly inject ons of 50 m lligrams of bismuth salicylate in oil were given intramuscularly and increased unt l the patient was receiving 100 milligrams weekly

By the end of the fifth week of this treatment the chest pain had entirely disappeared The full course was completed

The roentgen exam nation w s repeated in three months and showed a definite decrease in the size of the aorta (Fig 96B)

At the end of the first year of bismuth therapy the patient felt so well that she di continued treatment again against the advice of her physic an

In August 1932 two years later she reappeared complaining of slight pa n in the left chest An orthodiagram at this time showed l ttle change The electrocardiogram (F g 96C) showed only a left axis dev ation

B smuth therapy was again started and a full course g ven w th appropr te rest periods over the next thre years

Follow up exam nation in 1940 showed little change The patient remained free of symptoms She had lived a normal life in every espect s nce the d agnosis was made in 19 9

DISCUSSION Chest pain in a patient of this age who has a positive Wassermann reaction and roentgenographic evidence of aortic involve ment disqualifies her for neoarsphenamine unless preceded by a long preparatory period Many younger patients might show rapid improve ment in their lesion following administration of neoarsphenamine but the physician might later regret this therapeutic triumph in the presence of a failing heart

The relief of pain in older patients showing this degree of aortic involve ment is usually accomplished by persistent antisyphilitic treatment com bined with the proper amount of rest Where larger aneurysms are present and are accessible the procedure of wiring and electrolysis (page 229) proves helpful in relieving the pain The various procedures recommended

* Court sy of D Carroll S Wright

to block the nerves by *paravertebral injection* (page 256) are occasionally useful in the treatment of severe pain that attends aneurysmal growth

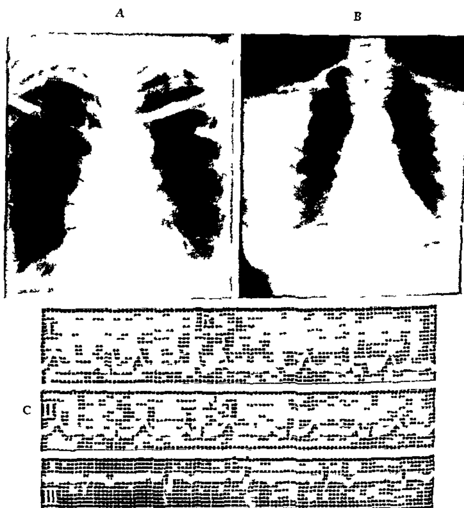



FIG 96 A Roentgen examination at beginning of treatment (19[illegible]9) Note increase in size first portion of aortic arch B Three months later Not decrease in size of the aorta

C The electrocardiogram (193[illegible]) showed a left axis deviation The other features like use normal for patient of this age Note the change in voltage of QRS3 caused by respiratory influence

The relief of pain when specific treatment was begun in this patient was evidence in favor of the diagnosis of syphilis Iodides in large doses are useful in early aneurysm An initial dose of 0 3 to 0 6 Gm (5 to 10 grains) three times daily was prescribed in this case and gradually raised to 4 0 Gm (60 grains) three times daily

The absence of cardiac enlargement and aortic insufficiency in this case when treatment was begun contributed in no small measure to the good result The aneurysm was recognized early and the patient aside from occasional lapses in treatment was able to follow an ideal regime She never had to work for her living consequently occupational stress and strain which are factors of importance in the production of large aneurysms in the male were entirely avoided It is doubtful if the same treatment in the case of an aortic lesion of similar extent and duration in a negro laborer would have the same happy result This is one reason I believe why various statistical studies differ with regard to efficacy of treatment at this stage of the disease

### Cardiovascular Syphilis—Aneurysm of Ascending Aorta—Survival for Three Years After Wiring

**Case 33** J G a negro laborer of 56 was admitted to the Philadelphia General Hospital complaining of shortness of breath and chest pain

History Marked dyspnea and pitting edema were present on admission Dysphagia and chest pain of intermittent character present for six months

Physical Examination B P 150 60 Obese deaf colored male Signs of old hemiplegia There was a large pulsating prominence the size of a lemon to the right of the sternum extending from the second rib to the fourth intercostal space (Fig 97A) There were systolic and diastolic murmurs over the base of the heart A tracheal tug was present The liver was 4 cm below the costal margin

Laboratory Data Wassermann reaction negative

Electrocardiogram left axis deviation Occasional premature beat of ventricular origin

Roentgenogram large aortic aneurysm

Course The aneurysm was wired twice with 15 feet of gold wire at intervals of two years The patient died suddenly from rupture of the aneurysm through the anterior chest wall

Autopsy (Fig 97B) The heart was enlarged with left ventricular hypertrophy The ascending aorta and the arch were dilated There was a large aneurysmal sac just anterior to the origin of the innominate artery which had eroded the second third and fourth costal cartilages and the right border of the sternum The sac was filled with organized thrombus and firm clot Coils of wire were recovered from the center In the descending aorta a second aneurysm was found just beginning to erode the body of the fourth thoracic vertebra The remainder of the aorta showed both luetic and atheromatous changes

### TREATMENT OF ANEURYSMS OF THE THORACIC AORTA

Discussion (Dr Henry D Jump*) The great majority of aortic aneurysms are due to syphilis The percentage will be found to vary in accordance with the observer and the consideration given to the history of infection the character of previous treatment the accuracy of the blood and spinal fluid examinations and the pathologic findings It may be accepted as a general rule that the farther from the heart aneurysms occur the lower will be the percentage that are caused by syphilis

From the nature of things the treatment of aneurysms is not very satisfactory and the most that we may expect to accomplish is palliation of

* Emeritus Professor of Applied Therapeutics Woman's Medical College of Pennsylvania




Fig. 9. A. Large aneurysmal sac presenting on anterior chest wall. B. Large aortic aneurysm. Note aortic dilatation and the presence of both atheromatous and syphilitic changes. (Autopsy No. 17 557, Philadelphia General Hospital.)

symptoms and a slight prolongation of life The vessel is usually badly diseased and another part may be expected to break down at any time Often multiple aneurysms are present

In the postmortem room saccular aneurysms are usually found partly filled with laminated clot The most of these have small orifices which cause slowing of blood current and favor coagulation Blackmore and King[30] found six in a series of 42 postmortem specimens of saccular aneurysms to be filled completely with clot of 19 fusiform aneurysms seven showed concentric clotting which had narrowed their lumen to a diameter equal to or less than that of the aorta With such evidence at hand of Nature s way of spontaneously eliminating these dangerous vascular dilatations we are prompted to devise methods that may be expected to aid her and if possible speed the process

The following measures have been advanced from time to time the introduction of needles into the aneurysmal sacs the application of a galvanic current to the outside of the aneurysms the placing around the vessel of constricting bands to slow the blood current a dry diet with prolonged rest the use of antisyphilitic drugs the introduction of wire and other substances and the anastomosis of the carotid artery and internal jugular vein Only the last four have survived and are occasionally useful in the modern treatment of properly selected cases

Inasmuch as early treatment produces far better results diagnosis of aneurysms in their incipiency is much to be desired This is not easy for often a positive history of syphilitic infection is not obtainable there are no positive serum reactions and there may be no symptoms On the other hand routine physical examination may reveal a suspicious area of supra cardiac dulness which the roentgen examination shows to be caused by a dilatation in the region of the aorta Under the fluoroscope this mass may be seen to pulsate or if the aneurysm contains much clot or is firmly tied down by an associated periaortitis or mediastinitis of syphilitic nature pulsations may be absent The administration of specific remedies may ultimately cause resolution of these tissues and permit pulsations to be observed

As the lesion develops other signs and symptoms occur bruit pressure and pain diastolic shock pulsation in the interspaces enlargement of superficial vessels of the chest hoarseness cough tracheal tug pulsus *differens etc*

The abdominal aortic aneurysm is always hard to detect even when large It usually lies high in the abdomen and percussion dulness may not be elicited in the back because of the overlying liver In this region pulsation is very deceptive for often a pulsating aorta in a thin individual may simulate the expansile pulsation of an aneurysm However if the hands can grasp the upper and lower poles of the sac an expansile pulsation will be detected and this common error avoided A roentgen study may likewise be of considerable help Erosion of the vertebrae may be present and if the

mural clot has become calcified this will outline the periphery quite clearly Under the fluoroscope *expansile pulsations may be seen*

DIET AND REST This regime of treatment was offered by Valsalva Bellingham and Tufnell of Dublin in turn The name of the last investigator is still attached to the method Complete physical and mental rest were planned in association with the very low diet The object was to concentrate the blood slow the heart rate, and reduce the arterial pressure in the hope that coagulation within the sac might be favored (Chapter 21)

The Tufnell diet is made up as follows

*Breakfast* two ounces of milk, two ounces of bread with a little butter

*Dinner* three ounces of meat without salt and four ounces of milk For a portion of the milk one or two ounces of claret may be substituted

*Supper* the same as breakfast

This severe program few patients can be induced to accept today, since the anemia and weakness which follow its prolonged use add little to the patient s comfort The addition of considerable protein and a little more liquids will make it more acceptable, and should not interfere with its purpose After all it is not unlikely that under this regime there is an increase in the mural clot which reinforces the wall of the sac Iodide of potassium was also given with this program to 'promote coagulation'

ANTISYPHILITIC DRUGS The treatment of syphilitic cardiovascular disease in general and the modifications called for in aneurysm have been discussed (page 219) A few important points, however will be repeated here for emphasis

Reactions to treatment should be avoided These therapeutic shock' (Jarisch Herxheimer reaction) and therapeutic paradox' (Wile) occur most frequently after the use of arsenicals Reactions may usually be avoided by beginning treatment with iodide and bismuth and continuing for 10 to 12 weeks Arsphenamine should never be used Neoarsphenamine has a place in the treatment of cardiovascular syphilis only after preliminary treatment with iodide and bismuth The dose of neoarsphenamine should be initially 0 025 or 0 05 Gm with a gradual increase weekly to a maximum of 0 3 Gm

In about 50 per cent of aneurysms this treatment has been followed by a relief of symptoms and probably a prolongation of life Arsenic affords a more certain relief from pain than iodide and the heavy metal This coincides with the observations of Moore et al and Padget and Moore [91] Moore and his co workers reported a mortality of 90 per cent among patients receiving little or no treatment and 40 per cent among those who had adequate treatment There was an average duration of life from the onset of symptoms of 19 months among the former and of 75 months among the latter The number of cases observed however was small Stokes [7] reports one case of aneurysm where roentgen ray examination showed only a dilatation of the aorta three years after continued treatment

In cardiovascular syphilis the serology is no guide to the efficacy of the treatment In only about 50 per cent of the cases is the reaction reversed

Heart failure occurs infrequently in aneurysm It may appear as a terminal event approximately 10 to 12 per cent die in this manner in contrast to 35 to 40 per cent who die of rupture of the aneurysmal sac When congestive failure occurs specific treatment should be discontinued and the cardiac symptoms treated in the usual manner with rest digitalization and mercurial diuretics However the chances of improvement when congestive failure becomes established are small

Wiring of Aortic Aneurysms The introduction of wire and the passage through it of a galvanic current for the purpose of coagulating the blood offer a measure of relief in selected cases of sacculated aneurysm In 1864 Moore suggested the introduction of filiform material into an aneurysm to produce clotting and he accomplished it in one case This pioneer investigator also stated that if wiring is to be done no artery should open from the aneurysm for if wire is exposed in a violent current of blood fibrinous clots will certainly break off from it and plug distant arteries He thus expressed the fundamental fact that only saccular aneurysms are susceptible to treatment by wiring

The next step was taken in 1879 by Corradi of Italy who used galvanic current through the wire he had introduced into a thoracic aneurysm There was marked relief for about three months The technic of Moore and Corradi has been the most acceptable and has been employed since its introduction Hare used it and reported a marked benefit in all of his cases although some had been in desperate condition previous to wiring Rosenstirn[3 3] reported a case in whom the improvement was remarkable A 25 year old patient had an aneurysm of the ascending arch which protruded on the chest Severe pain required heavy doses of opiates while oxygen was given for frequent spells of suffocation A few days after wiring the pain began to improve in two weeks dyspnea was relieved and in six weeks the pulsating tumor subsided Later he was reported to be in most excellent health to undergo any ordinary exercise He lived for 11 years and eight months following the introduction of the wire Rarely do such remarkable results occur but in the cases I have wired improvement in symptoms has always been observed

There were no changes in Hare's technic until Millar[29] experimenting with cats inserted *various kinds of wire into the aorta and found that zinc* caused a better coagulation of the blood than any other metal including gold and platinum He did not employ the galvanic current

Blackmore and King[30] devised an elaborate apparatus to introduce and coil a double strand of wire in the aneurysmal sac Their objects were to insert enough wire to slow the blood current and to heat this by an electric current to the point where the blood protein coagulates The coagulum that forms on the wire is difficult to scrape off This method was used in 11 cases with considerable success

INDICATIONS FOR WIRING Wiring is a procedure to be considered in saccular aneurysms only The object is to produce a clot in the aneurysm which will be attached to the wire and the wall and completely fill the sac If applied to fusiform aneurysms coagula which form on the coils of the wire may be swept off as emboli and lodge in distant vessels Moore pointed out this danger but in spite of his warning several fusiform aneurysms wired by the Moore Corradi method have been reported In each case emboli have formed and death has followed Blackmore and King have been able to use their method in the fusiform type of aneurysm with no untoward results

It was formerly stated that a thoracic aneurysm must protrude on the surface in order that a wire might be introduced with certainty into the sac However using a long needle guided by the fluoroscope it should be possible to reach those a slight distance below the surface In smaller aneurysms the results should be better for in these the aorta is less diseased than in the ones of larger size Even when blood oozes from the aneurysm that protrudes on the surface it may be successfully wired and external rupture delayed

The abdominal aneurysm must be exposed by celiotomy since few of them reach the surface I feel that the only indication for wiring the abdominal aneurysm is the great pain caused by their pressure on contiguous structures

CONTRAINDICATIONS TO WIRING When attacks of paroxysmal cardiac dyspnea are present the cases are almost hopeless and the operation of wiring will not postpone death Hare was of the opinion that the presence of more than one aneurysm was a contraindication The filling of one by a clot will deflect the blood current in such a manner as to increase the pressure in the other in which event rupture is *more apt to occur* For the same reason Hare believed that wiring should not be done in a saccular aneurysm which is distal to a fusiform

The equipment needed for wiring consists of

Solution of iodine 3 5 per cent
Alcohol
Hypodermic syringe and needles
*Hollow needle of about 0 gauge insulated with porcelain shellac or varnish except 5 mm (¼ inch) of the tip*
Wire of gold alloy (gold 60 per cent silver 30 per cent platinum 10 per cent—gauge 14)
Galvanic instrument with rheostat and milliammeter which is connected with house current or to six or eight dry cells
Oval metal pad 0 x 30 cm (8 x 10 inches) covered with cotton pad
Small scalpel
Rubber gloves
Gauze dressings sponges applicators collodion

The procedure is carried out under strict antiseptic precautions The wire is wound upon a spool and sterilized by heat For an aneurysm 7 cm (3 inches) in diameter (on the roentgen plate) two to three meters (7 to 10 feet) will suffice For an aneurysm 10

t 13 cm (4 to 5 inch s) in diameter three to four met rs (10 to 15 f t) will be t e[illegible]

Th ne dl also t rilız d by h at if it is insulat d with p rc lain If cover d with a heavy coat of varnish or shellac boil ng will soften this but it will harden when cooled Soaking in pure grain alcohol will sterilize it but part of the insulat on will go into solution

The operator and his assistant should ear rubber gloves and if the floor is not dry r bber soled sho s

After sterilizing th skin overlying the aneurysm ith iod ne and alcohol it is anesthetiz d w th 1 p r cent procaine solution and a s nall incis on is made through the sk n 1 to cm away from th thinnest part of the an urv mal wall The needle after being d pped into sterile water to lubricate it is quickly thrust through the incision into the aneurys n in a d rection away from the opening of the sac *Blood will spurt intermittently f om it immediately after the sac is entere l Until this oc urs the wire must not be introduced* If blo d does not appear and the needle is not occluded a longer needle may be needed in order to penetrat the lot in the margin of the aneurysm Puncture at another po nt may be useful in reach ng the nterior of the sac Feed the gold wire slow ly nto the sac unwind ng it carefully from the spool to prevent kink ng The *positive* pole of the battery i next attach d to the wire and the *negat ve* to the pad which has been previously moistened and put under the patient s back or buttocks or on the abdo nen Turn on the galvanic current slowly beginn ng at 5 milliamperes and c ease it 5 m ll amperes ev ry m nute until 45 to 50 milliamp res are being give Cont nu this amount for 10 minutes and then gradually withdra v the cur ent by reduci g 5 milliamperes every m nute Loosen the needle from the clot gradually and gently by turn ng and then slo ly withdraw t using counter pre sure on the sac Cut the wire close to the kin and push the end beneath t * Dress the puncture ith collod on o sterile pad of gauze There is rarely any leakage Follo ing w r ng the pat ent should be kept in bed for a period of at least two weeks to encourage consol dation of the lot

The results that may follow wiring of an aneurysm are

1 Pain lessens or disappears soon after the current is turned off
2 Other pressure symptoms are relieved when the size of the aneurysm decreases
3 The size of the aneurysm decreases when the clot consolidates and becomes organized
4 Rupture of the aneurysm is delayed or prevented in many cases and the patient s life prolonged

The prognosis varies with each case and depends entirely on the condition of the aorta No deaths are known which can be attributed to the procedure of wiring

* It is important th t the pat ent should not have access to the end of the gold wire This point as emphasized at a Philadelph a Gene al Hosp tal autopsy Dur g the pe iod when the s pply of the metal as lim ted Dr Jump sought to recover his wire from the n le of an aneurys n l sac When a careful search of the la ge firmly adherent clot as well a adj cent gions fa led to sho v any trace of the strand that had been fed n so generously nd tru t ngly the chemists we e hu riedly called n consultat on When the my tery deep d th physiolog ts we e summ ned However th wire had not been abso bed The b st l uth from th Social Ser ice Department retu n d the next day and upset all th hasty calculat ons He inve tig t ons revealed that the patient had f und the end of the w l arned its compos tio and p l t out ch by nch du ng frequent vis ts to a local tap room

W G L

In a few cases reported in literature, the wire has escaped from the sac and entered the aorta In one abdominal aneurysm on which I operated, the wire traveled upward until it reached the aortic orifice (Fig 98A and B) However, the patient's pain, which had been very severe was much relieved and the wandering strand of wire produced no untoward effects so far as we were able to determine The patient died 10 weeks later and we found at postmortem a rupture of the sac in the lower pole, which contained no clot The rest of the sac was well filled with a firm clot enmeshed in the wire There was no clot on the wire in the aorta and on close inspection no injury to the vessel was apparent

In recent years carotid jugular anastomosis has been the procedure of choice in the surgical treatment of aneurysm at the Philadelphia General




FIG 98 A Roentgen film showing coil of wire in aneurysmal sac B Same patient lateral view Note coil of wire in aorta as far as aortic valve

Hospital Since this procedure will be discussed in detail after the next case presentation my remarks concerning it will be few In 1930 McCarthy [4] reported ten cases and showed that the operation greatly relieves pain reduces the size of the aneurysm and postpones rupture In two of his cases where pressure symptoms recurred after primary relief I have resorted to wiring and in both, symptoms were again relieved In one patient a considerable reduction in the size of the aneurysm followed the wiring This major operation upon blood vessels that are the seat of advanced syphilitic disease in patients who are quite ill is less attractive to me than wiring The results are approximately the same following each procedure

### Cardiovascular Syphilis—Aneurysm of Aorta—Successful Carotid Jugular Anastomosis

**Case 34** Mrs M S age 59 was admitted to the Memorial Hospital on 1/5/39 complaining of smothering spells blood spitting pain in the chest and a persistent cough

History The patient was in good health until August 1938 when she had an attack of severe dyspnea followed by hemoptysis These symptoms subsided after rest in bed She had another attack in December 1938 About one week later she awoke at three o clock in the morning with a smothering feeling dyspnea and severe chest pain A hypodermic of morphine was required Following this seizure the patient was forced to remain in bed until she was admitted to the hospital Past history negative One child living and well No miscarriages

Physical examination revealed a well nourished elderly female propped up in bed coughing frequently and raising small quantities of blood streaked sputum

The left pupil was smaller than the right and did not react to light The carotid pulsation on the right side was quite noticeable No tracheal tug The chest was asymmetrical there was some bulging of the sternum at the second rib There was considerable widening of the area of supracardiac dulness

The heart was enlarged to the left The sounds were of poor quality the rhythm regular There was a systolic murmur at the cardiac apex another loud rough systolic murmur over the entire area of aortic dulness The blood pressure was 148/80

Laboratory Data Urinalysis revealed nothing abnormal Blood count R B C 4 040 000 W B C 6 650 hemoglobin 75 per cent (Sahli) N 50 M 7 F 1 B U N 9 mg per 100 cc of blood Glucose 100 mg The Wassermann reaction was four plus

Roentgen examination of the chest showed a heart enlarged in all diameters There was a large fusiform dilatation of the aortic arch mainly in its transverse and descending portions No erosion of the spine was evident in the lateral view

Clinical Diagnosis A Etiologic Syphilis Arteriosclerosis B Anatomic Cardiac enlargement Relative mitral insufficiency Syphilitic aortitis Aneurysm C Physiologic Normal sinus rhythm D Functional Classification Class 3 Therapeutic Classification Class E

Course Following a period of two weeks of bed rest during which time the patient was digitalized and given mercurial diuretics as required on 1/16/39 a left carotid jugular anastomosis was performed Her convalescence was uneventful Since operation there has been no hemoptysis dyspnea or pain

On 11/10/39 nearly a year later the patient reports no cough no pain and a marked increase in exercise tolerance B P 140/90 Bismuth and iodides were given during this period

Discussion (Dr James Lehman) In 1925 Babcock[18] described an operation for the relief of aneurysm of the arch of the aorta which has proved beneficial in many cases Heretofore all operations suggested or tried have been aimed at slowing or abolishing the flow of blood through the aneurysmal sac Carotid jugular anastomosis directs the arterial blood stream into the vein thus eliminating the peripheral bed of capillaries increasing the velocity of blood in the aneurysm and reducing the intravascular tension

It is a well known principle of hydrodynamics that a liquid moving through a tube under pressure exerts pressure against the wall of the tube inversely as the velocity through the tube As the lumen of the tube is constricted the velocity increases and the lateral pressure decreases Con

vessels as the lumen of the tube is increased the velocity decreases and the lateral pressure becomes greater It is the retardation of the flow of liquids through a tube that causes rupture not the high velocity Consequently when the aorta dilates to form an aneurysm the blood current is slowed and the wall of the aneurysm is subjected to much greater pressure than is the artery above or below this dilatation If it is possible to increase the velocity of the blood in the aorta and the aneurysm we should be able to decrease the lateral pressure on the wall of the sac sufficiently to prevent rupture

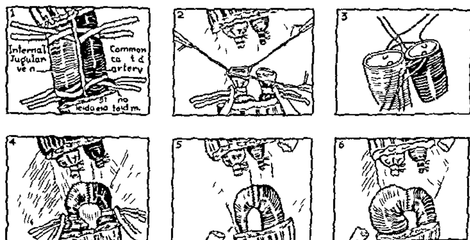



Fig 99 The steps in carotid jugular anastomosis

In 1930 McCarthy [1] reported ten cases operated upon by the Babcock method with gratifying results Since that time he has operated upon additional cases and states* that he has never observed rupture of an aneurysm following a carotid jugular anastomosis

The operation can be performed under local or light gas anesthesia The sternocleidomastoid muscle is divided transversely and the carotid sheath exposed Care should be taken not to injure the vagus nerve Umbilical tapes are placed above and below the point of anastomosis (Fig 99) The artery and vein are then divided and an end to-end anastomo is performed suturing intima to intima A second layer of reinforcing sutures should be placed to make the anastomosis secure The tapes are slowly removed and the wound closed in the usual manner

### Large Aneurysm of Transverse and Descending Aortic Arches—Onset with Backache and Pain in Left Arm—Arteriovenous Anastomosis Unsuccessful—Autopsy

Case 35 J G a colored laborer of 45 was admitted to the Philadelphia General Hospital complaining of pain in the left side of the chest and in the back of a year's duration

* Personal communication



Fig 100



Fig 101

Fig 100 Large aneurysmal sac involving the transverse and the descending portions of the aortic arch (Autopsy No 20 808 Philadelphia General Hospital )

Fig 101 Aneurysm of the descending thoracic aorta Note the erosion of the vertebrae with preservation of the intervertebral discs

HISTORY Patient unable to work for the past four months The pain started over the area of the left scapula and radiated to the left arm It was mad wor e by moving in bed and was relieved by lying on the right side Backache constant A loss of 20 pounds in six months was reported Untreated chancre 15 years before admis ion

PHYSICAL EXAMINATION Emaciated colored male of 45 B P 128/90 on the right and 60/0 on the left The radial pulse was weak on the left and full on the right side The pupils were small and fixed and did not respond to light The heart was not enlarged The sounds were of fair quality and a systolic thrill and systolic murmur were heard over the aortic area A was accentuated

LABORATORY DATA Electro ardiogram left axis deviation

Fluoroscopic examination dilatation of the aorta involving the transverse arch with slight dilatation of the ascending portion

CLINICAL DIAGNO IS A Etiologic Syphilis B Anatomic Aneurysm ascending and transverse arches C Physiologic Normal sinus rhythm D Functional Classification Class 4 Therapeutic Classification Class E

COURSE Anastomosis of the left carotid and jugular vein was performed Fourteen hours later the patient developed a right sided hemiplegia and died

AUTOPSY The aneurysm involv d the entire transv r e and descending portions of the aortic arch (Fig 100) The bodies of the second third and fourth vertebrae v ere eroded (Fig 101) The int rvertebral discs were preserved The spinal cord was exposed The orifice of the left subclavian was covered by extension of a large clot in the sac The heart was normal

**Discussion** Lucke and Rea [39] in a study of 249 cases of aneurysm found erosion of the vertebrae in 53 and spinal cord compression in one In a series of 100 cases reported by Brindley and Schwab [4] only one aneurysm was found to involve the spinal cord although a number eroded the vertebrae to some extent Shimkin[338] has lately emphasized the fact that compression of the spinal cord is a rare complication of syphilitic aortic aneurysm In the patient whose history appears above in spite of the marked erosion of the vertebral bodies no signs of spinal cord com pression were elicited

*The duration of life in these cases does not usually* exceed two years from the date of the onset of symptoms although occasional instances of exceptionally long survival appear in literature Considering the severity of the lesion and the pain that invariably attends the erosion it is sur prising how long these patients continue to work before applying for treatment This patient at the onset of his difficulty took a great deal of medicine for neuritis Failing to gain relief he went to a chiropractor who gave him a series of treatments When these made him wor e he went to bed where he obtained the most relief He had been in bed for four months without medical care when he was removed to the hospital Morphine in large doses was then required to control the pain

At the end of the first week an arteriovenous anastomosis of the left carotid artery and jugular vein was done under local anesthesia Pain ceased following the operation but 14 hours later the patient developed a right sided hemiplegia and died

# 7

# ANGINA PECTORIS

In medicine there are instances where the most profound human wisdom is unable to anticipate the course or predict the outcome — CORVISART (1808)

The term angina pectoris was first used by William Heberden in 1768 in referring to the symptom of chest pain of the type that was later (1788) shown by Edward Jenner to be associated with disease of the coronary arteries It is important to realize at the start that angina pectoris as its name implies is merely a symptom and not a separate disease entity While many terms exist to confuse the picture (stenocardia precordial pain anginal pain retrosternal pain) they all refer to a paroxysmal sense of constriction or pain of short duration in the upper chest that is produced by any factor increasing the cardiac burden and relieved by nitroglycerine or rest When we use vague terms like anginoid pain or pseudo angina we are only hiding our ignorance for these create a feeling of false security that hinders proper treatment

Consequently after a careful study of the patient we should form an opinion as to whether or not the pain in question is cardiac in origin Many times this opinion will have to be based entirely on the patient s story for the rest of the examination may be negative The sensation in the chest is described in various ways by different groups of patients Some refer to it as a constriction others call it a rawness or burning Whatever sensation is complained of inquiry should be made as to its nature following exertion The patient soon learns that the quickest relief comes with rest and consequently remains motionless during subsequent attacks It is not necessary to elicit a history of radiation of the pain to the shoulder or arm before a diagnosis of angina can be made for often there is no radiation the sensation being confined to the upper sternum In other cases there may be a typical radiation to the arms usually the left the side of the neck the jaw face and in rare instances the back If the pain is intense it may be felt in both arms although the left arm alone is more frequently affected The pain usually descends on the ulnar side of the arm and hand (Fig 102) and is followed by a feeling of numbness in this same region Occasional reference to the abdomen may cause difficulty in diagnosis (page 478)

While angina is commonly induced by exertion it may follow excitement anger heavy meals sudden exposure to cold or overindulgence in tobacco or coffee The presence of one or more of these precipitating factors

may at any time be responsible for the increase in the number and severity of the seizures

Attacks of angina follow no set rule The first attack may prove fatal or the issue may be deferred many years The pain may last a few seconds to a few minutes and in some patients may not cause a great deal of restriction in ordinary activities Angina may vary from a slight ache or constriction of the chest to a pain of great intensity depending on the sensitivity of the nervous system of the sufferer Some individuals experi-

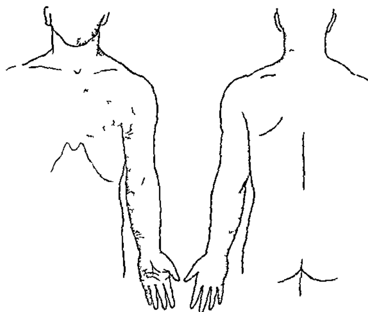


*Fig 10? The shaded areas in the diagram indicate the usual distribution of the* pain during an attack of angina pectoris (Redrawn from Diseases of the Heart Sir James Mackenzie London Oxford Univ Press 1918)

ence severe pain on the slightest provocation while in others the symptoms may be mild less easily produced and readily controlled However the possibility of sudden death during an attack should be borne in mind in all patients once the diagnosis *is established Some ambulatory patients* report many slight attacks each day and consume large quantities of nitroglycerine in their relief, others have fewer seizures There may in fact be long intervals of freedom from the symptom but recurrence is the general rule In rare cases angina disappears entirely (page 276) It is also possible for coronary disease to progress to an advanced stage without the appearance of angina on any occasion, in fact the majority of patients with coronary artery disease do not have angina

When the nature of the chest pain is evident the prognosis occasionally may be estimated by careful study of the patient at subsequent visits If

the anginal pain comes on more frequently and is induced by less exertion we can infer that increase in the degree of coronary sclerosis has probably occurred in which event the outlook is more serious Eventually attacks may be induced by the slightest stimulus even when the patient is resting Unusually severe pain of the type indicating occlusion of a branch of the coronary tree may replace the anginal pain in these patients at any time

## INCIDENCE

**Sex** Angina is much more apt to occur in men than in women, a fact that is constantly observed in all statistical studies

**Heredity** as every practitioner knows is another very important consideration in the diagnosis of angina The sudden death of either parent or of a near relative from angina or coronary disease is a vote in favor of the diagnosis of angina when the nature of the patient s chest pain is in doubt Obesity hypertension and diabetes are common accompanying factors that appear in the same family groups too often to be merely coincidental The overweight hypersthenic man or woman in middle life who usually has a ruddy glow of health and an abundance of energy is the anginal type When chest pain is complained of by these individuals it should always be carefully investigated

**The age** of the patient is another clue in the diagnosis Angina is rare (particularly in women) under the age of 40 in the absence of diabetes or hypertension It is more common after 40 and its greatest incidence is between 50 and 60 Angina may occur in young people but is very rare in the absence of an aortic lesion (page 255)

**Race and Occupation** The symptom is common among Hebrews and rare among Negroes It is much more apt to occur among executives and skilled workers especially where the duties are accompanied by the nervous tension so characteristic of our present urban existence Angina is not as frequently met among races where quieter living is the rule particularly in the tropical climates

## ETIOLOGY

As the clouds roll away from the many controversies concerning the etiology of angina that have filled the 150 years since Heberden s time the prevailing belief seems to be that it is caused by myocardial anoxemia But the skies have not entirely cleared since the work of some recent investigators does not fully agree with this theory In any event anoxemia of the heart muscle can most plausibly account for the majority of our present-day views Angina may be compared to the symptom that we call intermittent claudication that arises from the calf muscles on exertion when their blood supply is reduced The most common cause of myocardial anoxemia is progressive narrowing of the coronary arteries by an arteriosclerotic lesion The same interference to the blood supply can be

caused by spasm in younger individuals but it is doubtful if this element plays an important part in older patients whose hearts at autopsy are seen to contain rigid calcified coronary arteries Increase in the aortic tension was advanced by Albutt to explain angina, but it has now been shown that increase in the blood pressure in these cases is by no means a constant finding Wenckebach weighs the possibility of increased cardiac action in the absence of peripheral dilatation as the main cause of the anginal attack and he cites the action of nitroglycerine on the peripheral vessels as proof of his theory

**Syphilis** is a factor in the production of angina only when the luetic lesion extends down far enough in the aorta to involve and constrict the coronary openings Consequently syphilis explains only a very small per centage of the cases

**Aortic incompetence** from rheumatic disease may decrease the cor onary blood flow and give rise to angina in young people (see Case 39) In severe anemia the blood entering the coronary circulation is much reduced in hemoglobin If the caliber of the vessels is still further en croached upon by arteriosclerosis symptoms may appear when any unusual exertion is attempted However with advanced degrees of anemia the patient s general physical condition is such that he is usually not inclined to participate in severe forms of exercise and consequently the level where pain appears is seldom reached and rarely exceeded

**Thyroid Overaction** The increased metabolism that occurs in patients with thyrotoxicosis places an extra load on the circulation including the coronary arteries If a mild sclerotic change is already present but is insufficient to cause a deficiency in the blood supply to the myocardium this extra demand imposed by thyroid overaction may be just sufficient to cause the appearance of angina

We can now see the variety of factors that may be responsible for the production of the symptom that we refer to as angina pectoris Conditions arising in the heart itself in other organs at a distance from the heart or alterations in the blood picture provided the nervous mechanism of the patient is sensitive to stimuli arising from the area of myocardial ischemia may all be the cause at one time or another of anginal pain Since the pathways of these pain impulses from the heart have become better known attempts at blocking them by alcohol injections or surgical removal of vital segments have been attended by increasing success (page 256)

## DIAGNOSIS

Since angina is a symptom arising from a purely functional disturbance we should not be surprised when all methods of clinical examination yield negative results Many patients suffering from coronary insufficiency will show no increase in the cardiac size a normal blood pressure and an unaltered electrocardiogram If the course is complicated by the occurrence

of one or more coronary occlusions characteristic signs are very apt to be found in the physical examination and the electrocardiogram If hyper tension is present there may be cardiac hypertrophy relative mitral insufficiency and the other manifestations described in Chapter 9 Occa sionally if the electrocardiogram is taken during an anginal attack tran sient alterations in the RS T intervals or T waves may be revealed that are characteristic of coronary disease (Chapter 24)

## PROGNOSIS

If syphilitic heart disease is complicated by angina we can say at the start that the prognosis is poor (page 220) The ease of production of pain may be a guide to prognosis in a patient showing little evidence of nervous instability As a general rule the easier the production of pain the poorer the prognosis When typical anginal attacks occur while the patient is at rest the outlook is not good In White s series[39, 39c] the average duration of life from the onset of angina to death was well over five years Macken zie s study [40] showed a duration of 5 4 years On the whole it can be said that the average duration of life from the onset of angina to death of the patient lies somewhere between five and ten years Exceptions occur and in rare instances the syndrome disappears entirely Many patients who suffer from angina eventually succumb to other complications of their arteriosclerosis in the brain (cerebral hemorrhage) kidney (nephrosclero-sis) or lung (pneumonia)

## TREATMENT

Successful therapy in angina depends a great deal upon the influence of the physician on his patient In the beginning care should be used in statements made to the patient about the condition The situation can be satisfactorily and completely explained without using the word angina Emotions are closely associated with heart disease and of all words in the language capable of exciting them angina probably leads the list

**Regimen of Life** The management of no phase of heart disease will tax the ability of the physician more than cases of angina since the suf ferer must first of all be made to accept life with a handicap In those who possess the proper philosophy to do this gracefully life expectancy may be considerably increased The visits to the physician are in large part made for the supervision of this period of readjustment in the habits of living The patient is studied to ascertain what activities can be carried out with safety and how these coincide with earning a living The proper amount of exercise should always be encouraged while the dangerous phases of the day s program must be omitted no matter what the cost Here there can be no compromise A skilled physician will have his way and remain the respected adviser of the patient while the latter continues

to maintain the interest in life that is so essential if progress in treatment is to be made The physician must encourage and inspire the patient at all times yet be able to restrain him from engaging in harmful activities without too much emphasis on the limitations The practitioner who tells the patient nothing and continually describes the incurability of the condition to members of the family is not long retained

It is most important to follow a definite regime of treatment in all cases and this must be outlined to suit the individual needs of the patient Some thing new if sufficiently conservative should always be injected into any plan when it becomes monotonous Above all the patient should never be allowed to drift along as a chronic incurable case If the physician has succeeded in kindling the hope in the future at the first interview he is very much at fault if he does not strive to carry out his side of the contract at all subsequent visits

A careful scrutiny of the patient s daily routine usually brings to light the activities that most often provoke attacks These should be forbidden in constructing a program that is planned to allow all the exercise that may be tolerated without pain The patient should be instructed to stop and rest when he feels an attack coming on and no task should be started where this cannot be done If an attack is experienced that tends to persist in spite of rest and medication the patient should be told to return home and take no further exercise until seen by his physician

It may be impossible to re educate some patients to live quiet and orderly lives to go about their work slowly and deliberately, to take time with their meals to secure the proper amount of rest at night and to arrange periodic vacations away from business Other cases require time patience and all the tact that the physician can muster

**A well balanced diet** should be prescribed It is also important to regulate the amount of food especially when obesity is present In some cases food at frequent intervals may reduce the danger of overeating at meal times and serve the additional purpose of maintaining the blood sugar level at a top normal figure Protein restriction is unnecessary in patients suffering from angina unless the condition is complicated by an advanced renal lesion

The glucose and insulin regime has been popular in some clinics in recent years but I do not use it in the absence of diabetes In diabetic patients where insulin is required care should be taken to avoid hypoglycemic reactions that are attended by an increase in the anginal pain (page 287)

**Tobacco** has no place in the treatment of angina and should be avoided entirely if the seizures are frequent and severe[399] Coffee and tea may be allowed in moderate quantities Warm climates are preferable for vacations when these can be arranged Moderately high altitudes usually produce no increase in symptoms in the average patient but some react badly (page 250)

## Drugs

Nitrites The therapy of the attacks themselves in addition to rest consists in the use of one of the nitrite group These drugs act by their vasodilating effect both on the coronary circulation increasing its flow and on the other arteries decreasing resistance to the blood flow and thus lessening the work of the heart The action is peripheral and not on the vasomotor center Members of this group of drugs that are in common use today are amyl nitrite sodium nitrite erythrol tetranitrate and nitroglycerine The last two are organic nitrates but are reduced to nitrites in the body and consequently have a characteristic nitrite action All the nitrite drugs above mentioned have a similar action but differ in the time it takes for this action to become manifest in the body

Amyl nitrite possesses the quickest action It is a volatile liquid obtainable in ampules (2 cc ) and is administered by breaking the ampule in a handkerchief and inhaling the drug The effect appears in a few seconds reaches its maximum in about two minutes and passes off entirely in about ten minutes Amyl nitrite is rapidly absorbed into the blood stream from the lungs and quickly excreted It relieves the anginal attack at once but is less convenient than tablets of nitroglycerine and has the added disadvantage of attracting attention to the sufferer in crowded places where attacks are most likely to occur

Nitroglycerine tablets (dose 1/100 to 1/200 grain) are usually preferable as they are more easily carried can be taken under the tongue unnoticed and are less expensive than amyl nitrite ampules Nitroglycerine is absorbed from the mucous membranes of the mouth and acts in less than two minutes if a fresh friable tablet is used The effect may last an hour It is always well to start the patient on a triturate containing a smaller dose (1/200 to 1/400 grain) for occasionally certain individuals possess an idiosyncrasy to this drug If untoward effects in the form of throbbing in the head faintness headache or even syncope occur it is difficult to persuade the patient to repeat the tablet in any dosage when the anginal pain recurs

Sodium nitrite (dose ½ to 1 grain) given in tablet form by mouth acts more slowly (15 minutes) and for this reason has no place in the treatment of an attack of angina However its action is more prolonged lasting in some instances for two hours hence the drug is useful in prophylactic therapy

Erythrol tetranitrate (dose ¼ to ½ grain) is an even slower acting drug than sodium nitrite but the duration of its effect is three to four hours

All nitrites produce a vasodilating effect that may be readily observed in the skin vessels particularly of the face where the skin temperature is elevated The pulse rate rises following nitrite therapy but this is purely a secondary effect following the fall in the blood pressure The nitrites have no direct cardiac action I never use any of the group for the purpose of constantly maintaining a lowered blood pressure level

**Trichlorethylene** has been recently used in preventing attacks of angina in doses of 1 cc by inhalation [37] The action does not appear to be one of vasodilatation and no constant effect on coronary circulation in the experimental animal has been observed The drug has sedative and anesthetic properties and these probably account for its action It is inferior to the nitrites

***Alcohol*** *is an old remedy for angina still preferred by some who claim* that an ounce of whiskey or brandy has a speedier (and more satisfying) action The anginal attack vanishes as a sensation of warmth is produced by a dilation of the skin vessels The use of alcohol should be governed of course, by the frequency of the seizures experienced by the patient

**Routine Medication** The next question that arises after measures have been instituted to control the anginal attacks concerns routine medication Is there a drug that can be safely given over a long period of time that can be depended upon to decrease the frequency of the seizures? Again we meet the problem of the coronary dilator drugs and their efficiency *Following appropriate changes in the patient s daily regime it has* become the habit to prescribe one of the xanthine group of drugs I prefer theobromine sodium acetate in 0 3 Gm (5 grains) capsules after meals If after a trial of ten days the patient feels that the addition of this preparation has helped to decrease the number of attacks I continue it for a longer period If any symptoms arise from its use (nausea nervousness headache flatulence) it should be discontinued at once

While recently reviewing some clinic records of patients suffering from uncomplicated angina I found that the most popular prescriptions for these ambulatory cases are those containing one of the barbital preparations *Elixir* of phenobarbital with the occasional use of a purine derivative for a week or so and with nitroglycerine handy for attacks made up the regime of therapy in a large percentage of the cases A few physicians I discovered still cling to iodide medication supported by nitroglycerine when attacks occur Some patients in whom there is no reason to suspec syphilitic infection demand their drops at each clinic visit stating that the attacks are much worse when the iodide is discontinued The tremendous psychic factor present in many of the angina cases should not be overlooked when we attempt to evaluate this statement However there is no doubt about the fact that iodides in small doses over a long period *are less harmful than continued uncontrolled dosing with barbital preparations*

I have not used any of the various tissue extracts in the treatment of angina The nature of the substances my dislike of any form of injection treatment that brings the same group of patients back on the same days of the week and the lack of adequate controls evident in the literature have discouraged me at the start Other features of the treatment of angina that require fewer trips to the office are much more important Again a series of injections may act as a tremendous psychic stimulus to one group of patients making their evaluation difficult, if not impossible, while the

same treatment may cause another group to become weary of the physician and his regime The last group will end their visits and either continue without medical care or turn for treatment to one of the various cults The patients who continue treatment naturally make up in time a formidable group of cures but they are not representative of coronary disease and angina in any community and the physician by his over enthusiastic embrace of one method of therapy loses the opportunity of following many interesting cases The occasional patients who have unfortunately read about the value of the heart hormones in the daily papers are usually satisfied with the explanation of the status of this form of therapy

Digitalis is contraindicated in patients with uncomplicated angina (page 272) In some patients attacks may be increased in frequency following its use In the presence of congestive failure or auricular fibrillation that calls for digitalis anginal attacks, if formerly present commonly disappear

The physiotherapeutic measures of value in the treatment of angina will be found in Chapter 19

ABDOMINAL BELT
(See page 252)

ALCOHOL INJECTIONS
(See page 256)

EFFECTS OF AIR TRAVEL
(See page 250)

## ILLUSTRATIVE CASES

### CORONARY ARTERIOSCLEROSIS—MANAGEMENT OF ANGINA PECTORIS—THE QUESTION OF AIR TRAVEL

**Case 36** D C an advertising manager of 43 was first seen in June 1939 on which occasion the chief complaint was pain in the chest of a month s duration The pain was constricting in character always induced by exertion and relieved by rest nitroglycerine or whiskey No other symptoms referable to the cardiovascular system were present

THE PHYSICAL EXAMINATION showed nothing of significance B P 130/80 The heart was not enlarged The electrocardiogram however showed prolongation of the P R intervals When repeated after atropine the result was the same The Wassermann was negative and the blood count was normal

CLINICAL DIAGNOSIS A Etiologic Arteriosclerosis B Anatomic No cardiac enlargement Coronary sclerosis C Physiologic Anginal syndrome First stage heart block D Functional Classification Class 2 Therapeutic Classification Class C

**Discussion** In this case the diagnosis was made from the history alone The continued prolongation of the A V conduction time may be viewed in the light of a decreased blood supply to the bundle of His There may at one time have been an occlusion of one of the small branches of the right coronary artery with the production of a small infarct involving the septum The past history however failed to reveal any acute episodes of

chest pain that might have been caused by an occlusion However, the conduction defect produced no symptoms in this patient, and it was disregarded in planning the management

A review of this patient s daily regime showed habits of living that did not contribute to a successful control of the anginal seizures He was an executive in a large industrial concern and the nature of his position required him to spend most of his time traveling between branch offices in different parts of the country Since the distances were great air travel was almost always necessary This brings before us the question of permitting cardiac patients to be passengers on commercial air lines either for pleasure or when this method of transportation is essential for efficiency in business

Effects of Air Travel and Altitude on Patients with Heart Disease This problem has not been satisfactorily settled and will always have to be solved by a review of the circumstances present in each case A few general rules guiding this decision may, however, be stated The *important factors that have a bearing on the decision we give are the* cardiac status of the patient the distance of the flight contemplated the probable altitude and the previous experience of the patient with this form of travel During the past few years I have covered the entire route of several of the larger airlines in this country and have had first hand opportunity to observe passengers on large planes of the transcontinental type They are usually men in middle life or past middle life when the type of heart disease present is most apt to be coronary or hypertensive *It is probably not a coincidence that air travel has a greater* appeal to patients from these groups Speed and aggression become habitual and the air liner satisfies a compelling urge

Although close attention is paid to the physical condition of pilots and attendants on air lines there is little or no consideration given to the possible state of health of the passengers If this question arises at all it is referred to the family physician who renders the decision after an examination of the cardiovascular system However when we consider the number of passengers on air lines today and the few circulatory signs that are apparent on long distance flights the situation does not appear alarming Nevertheless there are exceptions and a few matters should be given careful consideration before granting the cardiac patient permission to travel by air

In the first place the anoxemia and the possible symptoms that may follow if the patient is kept for a long time at high altitudes in trans continental flights are by no means negligible The possible effect of air sickness on the circulatory apparatus must also be weighed since the incidence of this condition is great particularly when flying at low altitudes It is also well to ascertain if possible the effect of previous flights on the emotions If there has been no previous experience on which to render a decision the possible emotional upsets that may occur particu

larly in bad weather should be given due con ideration if the patient is known to have angina

Commercial air lines in the United States take passengers to altitudes varying between 4 000 to 10 000 feet During flight the passenger rests (weather permitting) in a very comfortable reclining chair The situation is totally different and consequently cannot be fairly compared to walking at a similar altitude With the patient resting comfortably altitudes reached by the plane have little effect on the normal circulatory apparatus Even at maximum elevations especially at night when the air is smooth and cool the effect may be most pleasant and even conducive to sleep Considering the number of older people who have all degrees of insuffi ciency of the coronary circulation if anoxemia had an extremely adverse effect we would hear about more fatalities during flight As the matter stands one air line reports but one fatality in flight due to cardiac failure in over 775 000 passengers Even this one accident was not believed to have been entirely caused by flying since the same incidence may occur in a similar number of persons selected at random on the ground

On the other hand in patients with slight or easily induced congestive failure the anoxemia of high altitudes is not recommended While it is entirely safe for the well-compen ated cardiac patient to sit or recline at a maximum altitude of 10 000 feet for a period not exceeding three hours it is unwise for the patient who has the slightest ign of congestive failure to assume this risk The same applies to patients with advanced degrees of coronary insufficiency who have severe angina While anoxemia may not be the factor in inducing attacks excitement and fear likewise enter into the picture and must be considered These patients should not be per mitted to travel by air

Only *a few studies have been carried out on the effect of different alti* tudes The majority of these seem to show a slight elevation of the pulse rate a maintained systolic blood pressure a drop in the diastolic level and an increase in the pulse pressure at high altitudes Increase in the respiratory rate at high altitudes may deplete the blood of carbon dioxide and if continued could produce a transient alkalosis Stratosphere and sub *stratosphere flying* particularly *in* transcontinental trips *will* bring *the* problem of anoxemia and its effect on the cardiac patient very much into the limelight in the future No doubt engineers and physiologists working together will soon devise a method of maintaining a uniform oxygen con tent in the plane with automatic adjustment to altitude

To summarize I believe that all patients with any of the signs of con gestive failure of recent origin or of long standing and patients who are subject to frequent attacks of angina should not be permitted to attempt flights of any distance This will include all class three and four patients (new classification) Patients in class two who suffer from advanced heart disease of any type and who experience dyspnea on slight effort should not be allowed to travel by air in rough weather or to take long transcontinental

flights They should also limit their flying to lines that do not go above 5,000 to 6 000 feet Class one patients after a short trial flight to allow the personal factors to be evaluated properly may be permitted to plan any trips by air provided that they restrict their flying to the large commercial lines

The patient under discussion was advised to accept another position with his firm at a slightly lower salary but one that did not entail long flights at frequent intervals His treatment was begun by a rest period of three weeks which was spent at the seashore During this time he was given triturates of nitroglycerine to take when needed for pain Routine medication consisted of a capsule containing phenobarbital 30 mg (½ grain), and theobromine sodium acetate 0 3 Gm (5 grains) after meals At the end of three weeks he was much improved and although the anginal pain was still present the attacks were not as frequent and were much less severe When re examined six months later the patient reported marked improvement in his condition Less tension was present in the new office, and there were greater intervals between attacks The only medication he was taking at this time was one nitroglycerine tablet as required

### Coronary Disease with Angina of Long Duration—Relieved by Abdominal Belt

**Case 37** Mrs R L a housewife of 65 was first seen in April 1935 complaining of pain in the left chest on exertion



Fig 103 Roentgen film showing cardiac enlargement of the hypertensive type Note enlargement of left ventricle Patient wearing belt

History Six years before the date of the first examination the patient began to have typical anginal seizures recurring frequently on exertion in cold weather and after heavy meals The attacks were relieved by rest or nitroglycerine

Physical Examination B P 110/80 Underweight Prominent abdomen The

rhythm was regular except for an occasional premature beat The heart was slightly enlarged (Fig 103) and a systolic murmur was heard over the apex and in the aortic area The aortic second sound was accentuated

LABORATORY DATA Wassermann reaction negative The electrocardiogram showed a left axis deviation The other features were normal Urine and blood count were normal

CLINICAL DIAGNOSIS A Etiologic Arteriosclerosis B Anatomic Slight cardiac enlargement Relative mitral insufficiency Coronary sclerosis C Physiologic Anginal syndrome Normal sinus rhythm D Functional Classification Class 3 Therapeutic Classification Class D

Discussion This patient used more nitroglycerine tablets for the relief of her anginal attacks than any patient that I have ever observed Daily averages of 36 triturates (1/100 grain) were not unusual during winter months No untoward effects were noted

Attacks of anginal pain occurred after meals on slight exertion on going outdoors on cold days and invariably followed emotional disturbances It was evident that some other form of treatment that would give additional relief would have to be sought I had previously used an abdominal belt of the type recommended by Kerr[188] with indifferent results in a small series of anginal cases However since the patient while not overweight had a prominent abdomen I decided to try again the effect on the anginal pain The belt was first applied in June 1939 when the patient was leaving for the seashore Three weeks later she returned very enthusiastic and stated that she had been able to walk the entire distance from her bungalow to the beach without stopping a distance of one half a mile In addition to this she was able to take other long walks at the shore without pain or dyspnea for the first time in years The number of nitroglycerine tablets required showed a sharp decrease during this period She continued to take a tablet or two after meals but this she admitted was more because of habit than actual pain

Many of the patients successfully treated by Kerr were overweight and had dyspnea in the upright position that was relieved in recumbency Viewed under the fluoroscope in the upright position the diaphragm was found to be one or two interspaces below the normal position and its movements were restricted In the recumbent position however a much greater diaphragmatic excursion was noted Kerr concluded that the abdominal viscera together with the increased accumulation of fat serve as a counter weight suspended from the diaphragm The belt restores the function of the diaphragm and aids in the return of the blood to the heart This promotes more adequate filling of the coronary vessels and accounts for the relief of the anginal pain

Kerr supplements the use of the abdominal belt with dietary restriction He hopes that this method of promoting more adequate filling of the heart might in some measure prevent or postpone coronary thrombosis Abdominal belts are also advised for sedentary workers chiefly males who are overweight in the hope of avoiding symptoms of insufficiency of the coronary circulation

So far I have not had uniformly good results following the use of the abdominal belt of the Kerr type in patients suffering from angina In this patient the application of the belt brought about prompt and marked relief For this reason I believe that my series of cases so far has been too small to be of value in giving a fair opinion in the matter No doubt my selection of the type of patient most suited for the application of an abdominal belt has been poor Consequently the following case report and discussion will serve as a better illustration of this new method in the treatment of angina

ARTERIOSCLEROTIC HEART DISEASE COMPLICATED BY ANGINA PECTORIS SEVERE VERTIGO, AND POOR POSTURE—SUCCESSFULLY TREATED BY APPLICATION OF ABDOMINAL BELT (PRESENTED BY DR. WILLIAM J KERR*)

**Case 38** *J D* a 61 year old white male was seen in the Medical Clinic to which he had come because of progressively severe precordial pain of eight years' duration The *pain radiated to the left shoulder and down the left arm was precipitated by* exertion and occasionally by excitement He had been seen repeatedly and all the usual measures for the relief of angina pectoris including the nitrites xanthines and extreme regulation of his daily routine had b n tried without avail He obtained relief from any single attack of pain by taking nitroglycerine *He had been digitalized because of mild congestive failure three years previously For six months prior to the present admission to the clinic he noticed progressive exertional dyspnea and severe progressive vertigo which was generally precipitated by his rising suddenly and changing his position quickly* This also came on *after he had been on his feet for a short time*

PHYSICAL EXAMINATION revealed a well developed slightly obese, adult white male with a drawn haggard facial expression appearing to be chronically ill Relevant physical findings were as follows

His posture was characterized by exaggeration of the *cervical thoracic and lumbar spinal curves The ribs were fixed in a slightly inspiratory position The head was thrust forward and the abdomen was protuberant and somewhat pendulous* The blood pressure in a reclining position was 130/86 mm of mercury When the patient stood the pressure changed to 178/? (it was impossible to determine satisfactorily the diastolic pressure) The heart was borderline in size on percussion with moderately good heart sounds The lung fields were clear Physical examination was otherwise essentially negative

*The electrocardiogram revealed evidence of myocardial damage compatible with* coronary occlusive disease The *circulation time in the standing position was* 32 seconds without abdominal support Following the application of an abdominal belt, the circulation *time changed to 21 ? seconds The blood pressure stabilized at* 13?/86 mm of mercury with the patient standing and wearing an abdominal belt Without support the patient was able to walk only ten yards at a military pace before the onset of anginal pain With a belt on he was able to travel 190 yards at the same pace without pain These determinations were made within five minutes of each other Studies in tidal air revealed an appreciable increase in the volume per respiration with abdominal support *Fluoroscopy showed a maximum diaphragmatic excursion of 1 5 cm in quiet* respiration With application of abdominal support the movement of the diaphragm increased to 3 cm The heart also seemed to decrease its amplitude of contraction with the patient's abdomen supported

This patient has been followed for six months during which time he has had only three or four attacks of angina These were all precipitated by excessive and ill advised exertion *He is now able to carry on ordinary activity with perfect freedom from pain* In addition he noticed instantaneous relief from his vertigo and this symptom has not returned His symptoms can be reprecipitated by removing his belt and subjecting h m

* Professor of Medicine University of California Medical School

to exercise It has n t been neces ary for him to use nitroglycerin at all since his abdomen was properly supported

### Angina Pectoris in a Child Secondary to Aortic Regurgitation of Rheumatic Origin

**Case 39** S P a colored girl of 1 was admitted to the Ph ladelphia General Hospital in January 1930 complaining of shortness of breath and attacks of pain in the region of the h art that radiated to the left arm At the age of 10 the patient had t vo attacks of rheumatic fever with severe joint manifestations A year before admission there was palpitation and dyspn a on exertion Nose bleeds were fr quent A month b fore ad mis ion chest pain was complained of following moderate exertion or excite ment These attacks rapidly increased in severity and frequency

Physical examination showed B P 140/40 Corrigan puls and marked pulsation of the vessels of the neck and arms The apex beat was in the anterior axillary line An ap cal diastolic thrill was palpable and presystolic and diastolic murmurs were heard over the mitral area The first heart sound was accentuated There was a loud diastolic murmur heard along the left sternal border

The electrocardiogram showed a left axis deviation and prominent P waves The T waves were upright The Wassermann was negative Blood count showed Red blood cells 3 200 000 White blood cells 15 000 Hemoglobin 68 per cent (Sahli)

Clinical Diagnosis A Etiologic Rheumati (inact ve) B Anatomic Cardiac enlargement Mitral stenos s mitral insufficiency Aortic insuffi iency C Physiologic Anginal syndrome D Functional Classification Class 3 Therapeutic Clas ificat on Class E

**Discussion** Angina pectoris in young people is rare When it occurs it is invariably associated with rheumatic heart disease and aortic regurgi tation White and Mudd[398] in 1927 collected 42 cases in patients under 30 years of age Stolkind in 1928 listed 29 cases Korns[194] and Levin [16] have reported single cases

Chest pain in young people associated with effort syndrome acute peri carditis or cardiac hypertrophy should not be confused with the type possessing the typical features of angina True anginal pain is sharper usually radiating to the left arm shoulder or left side of the face and is relieved by rest and nitroglycerine Exertion may show less direct rela tionship to pain production in young people than is usually the case in later years This child had attacks when at complete bed rest many came on during the night all were relieved by nitroglycerine

Many times in the presence of a free aortic leak angina occurs without any evidence of obstruction to the coronary flow that can be grossly demonstrated The low diastolic pressure that accompanies aortic regurgi tation has been stated as a likely cause of anginal pain However Hochrein has shown that the blood flow through the coronary arteries is modified chiefly by the work of the heart rather than by variations in the aortic perfusion pressure Laplace has also demonstrated that the incidence of angina in aortic valvular disease is not definitely related to the height of the diastolic pressure [0]

The prognosis of angina pectoris in younger patients depends on the degree of cardiac involvement and the complications of the rheumatic state and differs in this respect from the angina encountered later in life The

type of therapy that offers the most relief of the angina in young people for the longest period is sympathetic nerve block

PARAVERTEBRAL ALCOHOL INJECTION OF THE SYMPATHETICS IN THE TREATMENT OF ANGINA PECTORIS (Discussion by Dr C A Steiner*)

In 1916 Jonnesco[175] first treated angina pectoris by sympathectomy and recommended removal of the middle and lower cervical and the upper dorsal sympathetic ganglia Later various modifications of this procedure were devised by Leriche and Fontaine,[14] Coffey and Brown[69] White[391] and others

Paravertebral alcohol injections to relieve the pain of angina were first used in 1926 by Swetlow[368] who injected the upper dorsal ganglia The greater safety of this method has caused it largely to replace sympathectomy in the treatment of angina pectoris

It is assumed that the pain of angina pectoris originates in the heart itself and is transmitted from there to the central nervous system The better understanding of this method of transmission is mainly responsible for the greater degree of success obtained by surgical procedures today than was formerly possible

White[391] states that

> afferent impulses giving rise to the sensation of cardiac pain leave the heart by cardiac sympathetic nerve fibers coursing to the cervical and upper dorsal sympathetic ganglia but they all pass to the spinal cord through the rami communications of the upper five thoracic nerve roots as through the neck of a bottle

(Fig 104) Since these impulses may best be interrupted at the upper dorsal communicant rami or their ganglia the surgical attack is directed toward these levels

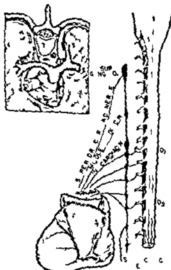
Obviously surgical measures must not be considered in the average patient suffering from angina pectoris whose symptoms are readily controlled by any of the forms of medical regime that have just been outlined They are however \ o thy of consideration in cases like this child where no response to adequate conservative treatment is evident, and where the frequent recurrence of severe attacks of pain in spite of medical treatment results in total disability Although dorsal sympathectomy is indicated where the risk is especially good alcohol injection is the procedure of choice in most instances No case need be denied the benefit of the latter procedure because of the severity of the cardiac lesion since the patients are not greatly disturbed by the injections

The purpose of paravertebral alcohol injections is to deposit a small quantity of 95 per cent alcohol in the immediate vicinity of each of the upper five thoracic sympathetic ganglia or their rami communicantes The destructive action of the alcohol produces a lasting interruption of the nerves carrying the painful stimuli from the heart

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Some idea of the nature of this procedure may be obtained from the following brief resume of the technic developed by James White[491] (Fig 105)

The patient lies on his side in his own bed with the head flexed and the knees drawn up The spine should be straight The bony landmarks are the spinous processes of the vertebrae the tip of each marking the level of the transverse process and posterior angle of the rib below After preparing the back a mark is made 3 to 4 cm directly lateral to each spine from the seventh cervical to the fourth dorsal vertebra Needles 8 to 10



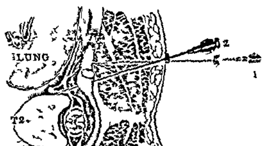



Fig 104 Fig 105

Fig 104 Diagram of the sympathetic nerves of the heart The direct thoracic cardiac nerves are shown joining the second third fourth and fifth thoracic ganglia with the posterior cardiac plexus (From The Autonomic Nervous System J C White New York Macmillan Company 1935 )

Fig 105 Paravertebral injection of thoracic sympathetic ganglia Method of inserting needles (*Ibid* )

cm long are inserted perpendicular to the back to a depth of 2 to 5 cm at which point they should be in contact with the transverse processes or ribs The lower borders of the ribs are determined the needles inclined slightly in a caudal direction and further inserted at an angle of about 20 degree toward the midline until bone is again felt approximately 3 cm beneath the ribs The needles should then be in contact with the lateral aspect of the vertebrae or the heads of the corresponding ribs

The sympathetic trunk lies at this depth running along the anterolateral aspects of the vertebrae and looping over the heads of the ribs Novocaine injected in this region will diffuse freely

through the retroperitoneal areolar tissue infiltrating the spinal nerves the communicant sympathetic rami and the gangliionated chain[391]

Making sure that the tip of the needle has not penetrated the pleural cavity a blood vessel or the subarachnoid space 2 cc of a 2 per cent novocaine adrenalin solution is injected through each needle Within 15 minutes characteristic signs of intercostal and sympathetic nerve paralysis (axillary anesthesia warmth of the arm etc ) should appear Then to insure complete anesthesia 2 or 3 cc of a 1 per cent novocaine solution is injected into each needle, followed by the slow instillation of 5 cc of 95 per cent alcohol

The patient should remain in the same position for at least an hour to allow the alcohol to become fixed in the tissues Usually the patient may get up on the following day and leave the hospital in three days

Sympathectomy is seldom used since alcohol injection can be performed with almost equal success and with much less risk However, when it is used the procedure of choice at present is the removal of the first second and third thoracic ganglia through a posterior approach, resecting the second rib

Obviously paravertebral alcohol injection can be safely and successfully carried out only by an operator who has had considerable previous training first in the anatomic laboratory and then as an assistant to a surgeon skilled in the method described above

The most troublesome complication following alcohol injection for the relief of angina is a painful intercostal neuritis which may persist for several months If the patient has obtained relief from the anginal seizures however this is seldom a matter of much consequence to him If the needle should accidentally pierce the pleura during its insertion pneumothorax may result but is rarely dangerous if promptly diagnosed and treated There is practically no mortality from the injection procedure itself, and even sympathectomy carries with it a very low risk if reserved for selected cases

Keeping in mind the fact that the cases of angina pectoris requiring surgery are usually the most serious ones the results are extremely good From the reports of James White[391] Paul White[393] Smithwick[316] Swetlow[368] Pletnev and Hesine[00] and others it appears that excellent results may be expected in about two thirds of the cases and marked improvement in about one half of the rest The relief obtained from either alcohol injection or sympathectomy is usually permanent

# 8

# CORONARY ARTERY DISEASE INCLUDING THROMBOSIS

This strange disease of modern life —MATTHEW ARNOLD *The Scholar Gypsy* Stanza 21

Angina pectoris and coronary thrombosis are both associated with coronary artery disease The former is a functional condition in which the blood supply to a section of cardiac muscle is temporarily deficient while

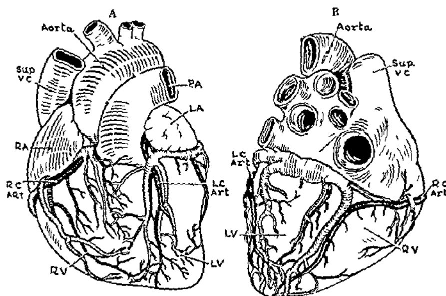



FIG 106 The great vessels coronary arteries and coronary veins A Front view B Base and diaphragmatic surface PA pulmonary artery Sup v c superior vena cava; R A right auricle L A left auricle; R C Art right coronary artery R V right ventricle L V left ventricle; L C Art left coronary artery

the latter is an organic lesion where the blood flow is permanently blocked by a clot and degenerative changes in the cardiac muscle ensue These dramatic episodes have focused a great deal of deserved attention in recent years on this typically American disease and a number of important advances have been made Electrocardiography has progressed to a point where not only is the diagnosis of occlusion of a coronary artery possible in 95 per cent of the instances but the site of the infarct can also

be accurately determined As we view our increasing knowledge with satisfaction many can still recall the day when thrombosis in the coronary tree was merely an interesting necropsy revelation Following Herrick s description in 1912 the importance frequency and clinical features of acute occlusion were established, and the modern physician has become skilled in its detection

In a series of 2877 consecutive autopsy reports studied by Levy [4] lesions of the coronary arteries were found in 25 9 per cent In half of these cases the involvement was slight or moderate causing no impairment of the coronary blood flow These autopsies covered a 22 year period and show a slight but steady increase in the incidence of the disease However it is most significant that diagnoses based on clinical observations alone have shown a greater increase in all clinics White [393] studying a group of 2 314 patients with heart disease in New England reports that 37 per cent were diagnosed coronary disease It is evident then that the diagnosis is much more often made during life than at autopsy in other words we are today acutely aware of the possibility of coronary disease, and its clinical signs and symptoms are seldom missed

## ETIOLOGY

Coronary artery disease causes cardiac damage by reducing the blood supply This may occur as a slow insidious process not reaching a degree sufficient to cause symptoms until late in life, or it may occur with dramatic suddenness at a much earlier age

**Arteriosclerosis** By far the most common etiologic factor in producing changes in the coronary tree is arteriosclerosis (Fig 107) It was present in over 95 per cent of Levy s series while syphilis was responsible in only a small percentage of the cases Much rarer causes of impairment of the blood supply to the myocardium are coronary embolism periarteritis nodosa and rheumatic coronary arteritis

The common arteriosclerotic lesion consists of abnormal thickening of the elements making up the intima of the vessel Areas of atheroma soon develop in many cases and these may soften rupture, and discharge their contents The rough areas that remain become suitable spots for the deposition of fibrin from the blood stream and a start is made for a thrombus which may rapidly develop where the vascular bed is narrowed and the circulation slowed

Inquiry into the cause of these fatal events in the coronary circulation would again lead us into a discussion of the theories that have been advanced to explain arteriosclerosis Suffice it to say that many times the stress and strain of modern life are reflected in the coronary tree Hyper tension if long continued exerts a harmful effect on the coronary arteries and the spot that bears the brunt of this burden and consequently the one apt to show the most change is the anterior descending branch of the

left coronary artery Hypertension may be influenced by environmental factors when the individual possesses the proper constitutional background In this event the tempo of modern life may after all have a decided influence on the speed with which coronary sclerosis develops Coronary accidents have replaced coma as the main causes of death among diabetics Here the endocrine imbalance resulting from the disturbance of the metabolism of fat and cholesterol plays a major role Finally the fact that we may inherit a tendency to early change in the structure of our arteries cannot be overlooked

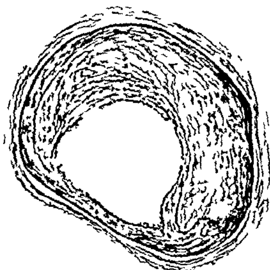


FIG 10 Atherosclerosis of a coronary artery

**Syphilis** has been shown to be no more frequent among patients with coronary disease than among those without it Syphilitic aortitis may involve the mouths of the coronaries and cause complete obstruction but damage of the coronary arteries themselves by syphilis is rare Likewise the part played by rheumatic infection in the production of coronary disease is obscure although we do know that involvement of the intima and media occasionally has been known to follow rheumatic infection with the subsequent formation of mycotic aneurysmal dilatations

**The role of focal infections** in the production of coronary disease is a much disputed and still unsettled point Likewise the relationship of coffee tea tobacco and alcohol to speeding the development of the sclerotic process cannot be said to be definitely established Emboli (air fat tumor cells fragments of vegetations) may occasionally invade the coronary arteries and produce infarction in patients of any age but this accident is rare

## INCIDENCE

**Age.** Arteriosclerosis of the coronary tree sufficient to produce clinical symptoms is uncommon under 40. After this age the incidence increases with advancing years, reaching its peak between the ages of 60 and 70. Bland and White[396] have shown that coronary thrombosis with infarction occurs at a younger age than coronary disease as a whole. The highest incidence of acute coronary thrombosis in their series occurred between 50 and 60 years of age.

**Sex.** Coronary disease is much more frequent among men than among women. All statistical studies confirm this statement, some reporting the ratio to be as high as seven to one. Occupation may have a direct relationship to this predominance of the male, since the overweight, overworked, overactive business or professional man of today is often the victim of coronary disease. Levy's studies have revealed that the largest percentage of cases of coronary sclerosis occur among foremen and skilled workers, with the professional and executive group taking second place.

## ANATOMY AND PATHOLOGY

An understanding of certain fundamental anatomic and pathologic facts concerning the coronary tree is essential to our discussion. In the first place, the coronary lesion may be microscopic, capable of producing no great reduction in the blood flow to the heart muscle; consequently no structural damage is evident and no clinical symptoms appear. However, if more marked narrowing occurs and thrombosis follows, the outcome will depend on the size of the artery occluded and on the extent and number of anastomotic branches that are present. These branches vary in different patients and at different periods of life in the same patient. As we grow older, the number of anastomoses in the coronary circulation increases, preparing us to withstand the accidents that may attend advancing years. If the process of narrowing is a more gradual one, these collateral pathways may develop to a remarkable degree, thus increasing the chances of survival when the occlusion finally becomes complete.

Sudden occlusions are not infrequent occurrences, in which crises all the cardiac reserve must be summoned for survival. In these emergencies, in addition to the collateral channels we have referred to, some circulation may be maintained through the thebesian vessels, which are small channels communicating directly with the interior of the heart. Blood vessels present in normal attachments of the pericardium likewise may be called upon to act as collateral channels. In emergencies even the small blood vessels in adhesions which may be present and bridge the pericardial sac often dilate and come to the aid of a failing coronary circulation. The Beck operation is based on the assumption that a transplant or

a bridge of pectoral muscle may be effective by augmenting the coronary supply in this manner

## DIAGNOSIS

It now becomes evident that the symptoms present in each patient will depend largely upon a number of variable factors and cannot be expected to be the same in every instance Occlusion of small arteries may take place with slight subjective manifestations It is quite likely that many times the incident is entirely overlooked since the cardiac balance is either little disturbed or quickly restored If a large artery is involved however, the clinical picture will be typical and the diagnosis may be made on inspection Between these two extremes the latent case on the one hand and the patient with a large occlusion on the other all gradations may be encountered Irrespective of the size of the infarct a great deal depends on the previous condition of the heart and whether or not a serious cardiac arrhythmia is precipitated by the accident

It is by no means an easy task to diagnose the latent case Subjective and objective evidence of the progress of the sclerosis may be entirely absent until thrombosis suddenly takes place It is likewise not uncommon to discover a markedly advanced coronary sclerosis at autopsy in a patient who died of some other disease If the coronary sclerosis advances slowly narrowing and finally obliterating many small end arteries the resulting infarcts heal and become invaded by fibrous tissue The myocardium then becomes progressively weaker and congestive failure may supervene and at autopsy the heart will show dilatation and much myocardial fibrosis Is this the heart lesion that we have been in the habit of referring to as chronic myocarditis If so it should be viewed in a different light since the fibrous tissue does not have its origin in an inflammatory process but is the end result of arteriosclerosis of the coronary arteries The cardiac dilatation that occurs usually causes stretching of the mitral ring before death and the systolic apical murmur of relative mitral regurgitation is frequently heard More advanced cases may show sclerosis of the valvular structures and the regurgitation may then be a combination of these two factors

**Cardiac failure** may be gradual in its onset As the blood supply to the heart muscle is slowly curtailed dyspnea appears on less exertion Edema of the feet may be present at night and finally attacks of cardiac asthma or cardiac dyspnea give evidence of a diminished myocardial reserve Pulmonary edema congestion of the liver and other signs may be added to the picture at this stage

**Cardiac Irregularities** The small infarcts in the myocardium that undergo healing may act as irritable foci and their presence may then be made known by the occurrence of the frequent premature beats that interrupt the cardiac rhythm Paroxysms of tachycardia from a succession of these stimuli may be precipitated by a sudden occlusion The onset of

chronic auricular fibrillation is not uncommon as the involvement of the auricular muscle advances Occlusion, gradual or sudden of the artery that supplies the bundle of His may cause delay in the passage of the impulse for cardiac contraction from auricle to ventricle (Case 36) Sudden occlusion of this artery may cause complete heart block I have seen Adams Stokes seizures occur following an attack of chest pain and a drop in the ventricular rate to 40 Pulsus alternans may be evident in patients with a sudden thrombosis or in cases where chronic failure has progressed to its terminal stages and the ventricular muscle is making its final struggle to survive by partitioning its remaining reserve strength

**Gastro intestinal Symptoms** Sometimes as Riesman has shown[314] the symptoms produced by advancing sclerosis of the coronary arteries may be entirely gastro-intestinal This is not surprising when we consider the fact that the vagus nerve supplies both the heart and the alimentary tract Consequently abnormal states of the heart may be reflected in the group of symptoms often referred to by the patient as indigestion' A similar reflex from the stomach to the coronary tree may be possible this pathway may account for attacks of pain or even occlusions that occur too frequently after eating to be merely co incidental Many patients who reflect the signs of advancing heart disease in chronic gastro intestinal complaints are often treated for gallbladder disease (page 479) Even the pain of an acute occlusion may have an abdominal reference and if attended by nausea and vomiting the differential diagnosis may be difficult (Case 101) It is small wonder that many attacks of coronary occlusion masquerade under the term acute indigestion

**Chest Pain** As the coronary lesion progresses a prominent symptom is chest pain it occurs usually in paroxysms and is the direct result of myocardial ischemia This cardiac pain may come on after emotion or excite ment but is nearly always induced by exertion particularly when the patient hurries up a slight grade It is also accentuated by cold weather and by overeating The pain may be of the constricting type and remain con fined to the front of the chest or it may radiate to the left arm both arms the neck or the jaw bone When it travels down the arm it is usually on the ulnar side and is felt in the ring and little fingers A reverse direction of the pain may be met in some patients in which event it starts in the arm or elbow and radiates toward the shoulder The intensity of the pain of angina varies according to the individual It may be quite typical in onset and distribution in some while in others it may be expressed as a slight ache in a tooth a finger or an elbow Nevertheless the pain carries the same significance in all Some patients will describe the sensation that accompanies narrowing of the coronary arteries as a constriction or tighten ing and will object to the use of the term 'pain' However this in no way detracts from the seriousness of the symptom Cardiac pain nearly always plays a prominent role in the symptomatology of those whose daily activi ties are greatest particularly if these activities are attended by emotional strain An attack may last a few seconds to a few minutes and is usually

relieved or at least greatly improved on rest (For a more complete discussion of this symptom, see Chapter 7)

**Thrombosis** As sclerosis of the coronary vessels progresses thrombosis may occur (Fig 108) The signs and symptoms attending the occlusion of a large vessel by a thrombus are well known Pain usually appears suddenly and increases until it becomes agonizing in its intensity It is usually substernal but may radiate to the epigastrium and be followed by nausea and vomiting When the infarct is large the patient is extremely pale and has the appearance of one acutely if not mortally ill A cold sweat appears the blood pressure drops and the pulse may for a time be weak and almost imperceptible Often in patients where the lesion is one of long duration and anginal pain a daily occurrence the attack may not present the textbook picture of pain and collapse but may be ushered in by a paroxysm of dyspnea pulmonary edema or congestive failure symptoms that characterize advanced coronary sclerosis In other patients subject to angina, a thrombotic occlusion may occur following an increase in the number and severity of the anginal attacks The pain of the occlusion is more severe and longer in duration than the pain of angina and does not yield to nitroglycerin

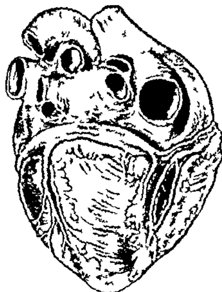


Fig 108 Posterior descending branch of the right coronary artery incised showing presence of an obstructive coagulum The diagnosis of thrombus was made by section

If the obstruction occurs in a vessel on the anterior surface of the heart, a friction rub may be heard over the localized area of pericarditis while if the infarct faces posteriorly this valuable sign is not elicited The absence of a precordial friction rub following acute chest pain however does not rule out an anterior occlusion

Since the infarct is in reality an area of necrotic material in the heart wall an elevation of temperature commonly follows its formation Leukocytosis likewise appears and the red blood cells show an increase in their rate of sedimentation

If the infarcted area extends to the inside of the ventricle the necrotic surface encourages the deposition of fibrin and a mural thrombus may appear parts of which may subsequently become dislodged and act as emboli Those originating in the right ventricle lodge in the lungs while

those dislodged from the left side of the heart (Fig 109) come to rest at points in the systemic circulation the brain, the spleen the kidney the



Fig 109 Mural thrombus at site of cardiac infarct (marked by arrow) (Autop ) No 3 190 Philadelphia General Hospital )

mesenteric vessels or the extremities Embolism is a frequent cause of sudden death following a coronary artery occlusion that is often overlooked It is more common than cardiac rupture When coronary occlusion

is suspected or when it occurs in the absence of pain and the possibility of a mural thrombus is not considered, a primary brain or pulmonary lesion may be diagnosed. Consequently embolic manifestations that suddenly appear in other organs of the body should always prompt us to investigate the integrity of the coronary tree.

Following acute occlusion a number of cardiac irregularities may appear. The most serious among these are paroxysmal ventricular tachycardia and ventricular fibrillation. In many cases where large occlusions occur the immediate onset of ventricular fibrillation usually ends the picture.

**Aneurysm.** If the patient survives the initial shock of the coronary accident and the blood pressure again mounts, all danger is not over. Unless care is used in management a cardiac aneurysm, which is merely a localized bulging of the heart wall, may form at the site of the infarction (Fig. 110). If the patient's activities are resumed too soon after a large occlusion, rupture of the heart wall through the infarcted area may occur. Any sudden exertion or strain during the period of bed rest may also produce the same result.

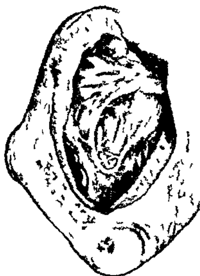


Fig. 110. Cardiac aneurysms

This is the classical picture of coronary disease ending in thrombotic occlusion of branches of the coronary artery. The symptoms point to the progress of the underlying lesion and the therapeutic implications are clear. However, not every case is so easily recognized. Where little interference with normal coronary flow is produced, symptoms may be entirely absent until the first occlusion suddenly appears. The presence of coronary disease should be suspected in any patient over 40 who complains of dyspnea or chest pain, particularly if this patient is an obese male. A positive family history or the presence of hypertension should strengthen the suspicion. Many times the electrocardiogram proves a valuable help if suggestive changes are seen. On the other hand, a negative electrocardiogram does not eliminate the possibility, since minor alterations in the blood flow in the absence of acute myocardial infarction produce no marked abnormality. If the patient is seen soon after the onset of a small occlusion, a normal tracing may be obtained. Consequently a repetition of the test in a few hours is advisable, since this may show significant alterations (page 643). Usually any marked changes that occur in the features of the electrocardiogram from day to day in a person who gives enough of a history to arouse suspicion of the presence of a small occlusion may be attributed to

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Fig 109 Mural thrombus at site of cardiac infarct (marked by arrow) (Autopsy No 390 Philadelphia General Hospital)

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Fig 110 Cardiac aneurysm

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this cause and are valuable in reaching a final diagnosis It is important to recognize the mild cases and establish proper treatment early Few of the *characteristic clinical signs such as low blood pressure, fever leukocytosis* and shock may be evident in which event the electrocardiogram assumes a place of great importance in diagnosis

Severe grades of anemia may produce chest pain as a result of myocardial anoxemia In most of these cases it is quite likely that some degree of coronary sclerosis already exists and the addition of the anemia is enough to precipitate symptoms of insufficiency In the same manner hyperthyroidism by increasing the metabolism may place just enough added strain on already diseased coronaries to produce attacks of anginal pain A similar strain on the coronary circulation may occur in older patients with the onset of paroxysms of tachycardia flutter or fibrillation

Levy has called attention to the production of chest pain simulating coronary occlusion that may occur in persons consuming large quantities of tea or coffee Tobacco may likewise aggravate the symptoms of coronary disease [40, 399] Chest pain often accompanies effort syndrome but here the other features of the examination are usually sufficient to make the distinction

The chest pain and precordial friction that accompany acute fibrinous pericarditis are rarely confused with coronary thrombosis The age of the patient and the signs of infectious carditis may serve to make the distinction although the features of the electrocardiogram in the two instances may be quite similar (see Fig 252)

## PROGNOSIS

The prognosis of coronary disease is variable Many times the condition is discovered *in old people at postmortem* In direct contrast to the long symptom free existence possible in some of these cases there are instances in younger individuals where a thrombus forming on a single plaque in a large artery may spell quick disaster In between these two extremes there are numerous cases where the diagnosis may be made and successful treatment carried out over a long period Much of course depends on the patient s intelligence nervous temperament and willingness to co-operate Some apparently hopeless cases (page 278) may be carried successfully over a period of years with no increase in symptoms and in some instances even *an improvement in the exercise tolerance may be observed* Patients with syphilitic aortitis who have involvement of the coronary arteries at their site of origin do poorly and generally succumb at an early age Hyperthyroidism accentuates the symptoms of coronary disease but if successfully managed the outlook is good for after thyroidectomy the symptoms of coronary sclerosis may again retreat below the clinical horizon and remain out of the picture for years As a rule progress of the coronary lesion may be roughly gauged by the ease of production of anginal pain when this symptom is present Increasing narrowing of the coronaries is reflected in

the patient's complaint that the pain appears on less exertion Finally pain appearing on the slightest exertion or while at rest suggests an advanced lesion and a poor prognosis † Some patients following a typical history of angina may have an occlusion and subsequently when ordinary activity is again attempted have no reappearance of anginal pain (see Case 40) Here we can infer that the artery occluded and the area of muscle it supplied were the only sources of painful afferent stimuli arising from the heart Prognosis in these cases should be excellent

Occasionally autopsy reveals only a very small coronary occlusion that appears insufficient to account for the fatal outcome In these cases death probably results from the reflex spasm produced in neighboring coronary vessels by the occlusion This increases the area of ischemia and precipitates fatal ventricular fibrillation Reflexes from the gastrointestinal tract following a heavy meal may also produce similar fatal spasms of coronary branches Consequently we cannot say that all small occlusions in their early stages are invariably associated with good prognoses



Fig 111 Atheroma of the abdominal aorta

While the occurrence of coronary thrombosis is a serious complication in coronary disease it does not necessarily lead to a poor prognosis White has reported several instances of long survival following a proved occlusion One patient[394] survived 24 years and another 17½ years

## TREATMENT

### General Principles

The objects of therapy in coronary disease are to relieve the pain of angina or occlusion and to establish a satisfactory daily regime in order to postpone for as long as possible heart failure either of the congestive or

coronary type As we shall see in the discussion of the treatment of the cases that follow each patient presents problems demanding individual attention Coronary disease is chronic and slowly progressive There is no specific regime of therapy unless the involvement is secondary to syphilis The physician therefore meets all the handicaps and situations that occur in the management of any patient of this age group who has a chronic disease

At the start the patient must be willing to accept certain restrictions in his activity in return for a less demonstrative coronary circulation No difficulty may be encountered if the patient s confidence is gained in the beginning by frankly stating the situation in simple terms and explaining the action of the few drugs prescribed This may be a time-consuming procedure but it pays dividends in the end for a skillful physician may keep his patient s outlook on life unchanged in the face of advancing lesions Every detail of the day s program should be reviewed from the time that the patient gets up in the morning until he goes to bed at night This should include what he eats where he eats and the time allowed in the process No happenings in the course of the day should be considered too trivial to be included in this review and weighed in the light of the possible effect they may have on the coronary circulation

The questions that the patient asks the physician will depend a great deal on the patient s station in life these questions should always be answered with this circumstance in mind Usually enough has been learned by the time the interview ends to guide the physician in his answers The patient s nearest relative should always be given full information in regard to the exact state of affairs and the fact should be emphasized that a patient with coronary disease and angina may live for years but sudden death at any time always remains a possibility

If the patient is free of symptoms but shows evidence on clinical or laboratory examination of the presence of coronary disease this rearrangement of the regime proper dietary management (page 541) and removal of obvious foci of infection constitute all the necessary measures The administration of iodide of potassium in doses of 5 to 10 grains (0 3 to 0 65 Gm ) three times a day appears to be a time honored procedure Some claim that this drug inhibits vascular spasm others that it inhibits the advance of the arteriosclerotic process that is favored by high cholesterol diets others that its action comes about through a change in the viscosity *of the blood but* most physicians when questioned are usually at a loss to explain its rationale If the Wassermann reaction is negative and hyperthyroidism is absent I fear that the iodides have gained most of their reputation by coming to the rescue when no other remedy appears definitely indicated

## DRUGS

**Xanthines** The use of the xanthines as dilators in disease of the coronary arteries is a valuable addition to our therapy Three alkaloids are

included in the caffeine group caffeine (trimethyl xanthine) theobromine and theophylline (dimethyl xanthine) all are purines and therefore closely related to uric acid These substances are insoluble in water but when combined with salts like sodium salicylate sodium acetate or ethylene diamine they become soluble and in this form acquire a wider range of clinical usefulness The most popular member of the group is theophylline ethylene diamine (aminophylline euphyllin or metaphyllin) In experimental work on laboratory animals most observers agree that the coronary arteries are dilated by the drugs of this group [104, 113, 120] Even when administered in great dilution to isolated hearts the coronary output increases 50 per cent Cushny suggests that the effect may follow a direct stimulation of the heart muscle However uniformity of opinion as to the effect of the xanthines in man is still lacking Some clinicians find them extremely useful in increasing the blood supply to the myocardium Experimental proof of this stand may be found in the work of Fowler and his associates[104] who administered aminophylline to normal dogs after ligation of a coronary branch and found that the resulting infarct was smaller than *in control dogs where the drug was not used However it is only fair to* state that similar results were not obtained by Gold and his workers Wiggers and Green likewise found the xanthine group ineffective in increasing the coronary flow in dogs after experimental coronary occlusion [119, 120]

Taking into consideration the variable factors that exist in every case of coronary disease in man a definite decision concerning the value of the xanthines is difficult to obtain While I do not doubt the good results reported in the literature by many observers I have not learned to depend on these drugs so much to relieve or prevent pain in coronary disease as I have for their diuretic action in cases of congestive failure and in the treatment of certain types of dyspnea where morphine is poorly tolerated

Another point against the wholesale use of the xanthines is the expense to the patient The best rule in practice is to administer one of the group for example theobromine sodium acetate in 0 3 Gm (5 grain) doses after meals for a period of a week If there is no definite improvement in the symptoms it may be discontinued Considering the rigid calcified coronaries that we see so often at autopsy I doubt the efficacy of these drugs as dilators in every case However they may be efficient in the treatment of coronary disease in younger patients where reflex spasm of the vessels still plays a major role

Barbiturates At the present time sedatives of the barbituric acid series are very popular in the treatment of coronary disease particularly when associated with hypertension While there is no doubt that these drugs serve to allay fear relieve insomnia and nervousness and by blocking reflex pathways reduce the number and severity of anginal attacks they should be used with care and their administration should be continuous only when the patient is under the constant supervision of the physician Untoward symptoms are not uncommon while in excessive doses these drugs can do harm It is wise not to exceed 15 to 30 mg (¼ to ½ grain)

of phenobarbital three times daily A mild sedative effect is usually obtained by this dose, which is valuable in quieting the heart and decreasing the incidence of ectopic rhythms

**Digitalis** Recent studie all seem to confirm the opinion that digitalis is of questionable benefit in cases of coronary disease in the absence of signs of congestive failure Ginsberg and his associates[116] studied the effect of various digitalis preparations on the coronary sinus outflow of heart lung preparations and of intact dogs They observed an initial decrease in the coronary flow lasting about ten minutes which was generally followed by an increase for the remainder of the experiment Variable results were obtained in intact animals many showing no change at all in the coronary flow following digitalis administration These carefully performed experiments indicate that the constrictor effect of digitalis upon coronary circulation is not sufficient to contraindicate its use unless there is present an extreme deficiency in the coronary flow Travell et al[375] studied the effect of digitalis on cats three weeks after experimental ligation of a coronary vessel and found all the animals were more susceptible to digitalis than normal controls About three fourths as much digitalis was needed after ligation of a coronary vessel to cause a ventricular ectopic rhythm and death As a rule they found that the larger the infarct, the more susceptible the animal appeared to be to the drug but many exceptions were noted These investigators concluded that digitalis administered after coronary occlusion at least in the experimental animal favors the production of abnormal impulses in the infarcted area that may lead to attacks of ventricular tachycardia and fibrillation In view of these results the best rule to follow in practice is to withhold digitalis in coronary di ease in the absence of signs of congestive failure With the appearance of cardiac decompensation however digitalis should always be given in sufficient amounts to achieve a therapeutic result (Chapter 2)

**Nitrites** should be used as required for the anginal pain that may complicate coronary disease Fresh nitroglycerine triturates (1/100 grain) dissolved under the tongue as occasion demands still constitute the best form of nitrite therapy The tablets should never be prescribed to be taken at stated intervals during the day Occasionally good results may be obtained by using a tablet just before an activity that previously provoked an anginal attack In this way it may be possible to open up some collateral channels in the coronary circulation by combining the dilating effect of the drug with the increased blood flow that follows the exertion A further discussion of nitrite therapy will be found in Chapter 7

## MANAGEMENT OF ACUTE OCCLUSION

**Control of Pain** The first thought is to control the pain which is usually of a severe agonizing variety Consequently a hypodermic injection of morphine sulfate ¼ grain (15 mg) should be given at once Continuation of the pain calls for a similar dose in a half hour and in some cases several hypodermic injections may be required If possible the patient

should be made comfortable where he is found by the physician on his arrival for it is distinctly harmful to move a patient in this condition unless it is an absolute necessity The patient should not be undressed until some degree of recovery is evident in the appearance pulse and blood pressure The application of local heat is advisable in the form of a hot water bottle or electric pad At this stage it is unwise to use a multiplicity of restorative measures The acute insult to the myocardium contra indicates the use of large infusions that may add to the circulatory load It is also better policy to withhold adrenalin and ephedrine unless the emergency is extreme and the patient is unconscious and pulseless

**Absolute physical and mental rest** are essential for the patient and are usually obtainable only when tasks are found in some other location for the excess number of anxious relatives that usually crowd the scene It is far better to engage a capable attendant at the start The type of bed and other matters relating to the general care of the patient with failure of the coronary circulation do not differ from those recommended for failure of the congestive type (page 74)

Once the diagnosis is established too frequent examinations disturb the patient A trip to the hospital to secure an electrocardiogram or roentgenogram to prove what is obvious on clinical examination is likewise no great advantage at this stage of the treatment

When the pain has been completely controlled the hypodermics of morphine should be stopped Enough sedation should be given however to insure a good rest during the first few nights of the illness It is quite possible that the morphine in some patients may induce vomiting so it is wise to discontinue it as soon as the pain disappears and use as a substitute for allaying restlessness one of the barbituric acid derivatives or sodium bromide Sedatives are necessary in securing the relaxation that is so essential during the first few days following an acute attack of coronary thrombosis Since nausea and vomiting may accompany the state of shock that attends the accident or may follow the large doses of morphine the diet for the first day or two will not be a matter of great concern (Chapter 21)

**Constipation** usually follows the morphine but may be disregarded during the first two days unless a great deal of distention develops in which event an enema is indicated It is wise whenever possible to postpone the use of enemas until complete circulatory balance has been restored and the patient is definitely on the road to recovery Later in the course of treatment a routine laxative sufficient to secure one bowel movement daily should be given and the patient instructed to avoid straining at all times

**Oxygen** In many cases following occlusion of a large coronary branch cardiac action is much embarrassed and life hangs in the balance Survival in these instances will depend largely on the aid rendered by the physician and the speed with which he acts Often the administration of oxygen may prove the deciding factor in swinging the balance in favor of recovery

In patients who show marked dyspnea and cyanosis oxygen is best given in a concentration of 45 to 50 per cent using a tent but other methods if intelligently used should prove equally efficient (page 99) Oxygen brings prompt relief to the respiratory embarrassment and restlessness, diminishes or abolishes the cyanosis, and slows the cardiac and respiratory rates[11 17] Levy and Barach[1 3] recommend the use of an oxygen tent over long periods for patients suffering from acute attacks of coronary occlusion If the patient is removed from the tent too soon, the symptoms of circulatory distress may recur

**Glucose** If we continue to plan our treatment physiologically we should next attempt to make more glucose immediately available to the overtaxed heart muscle All laboratory workers have witnessed the prompt revival of the isolated heart of the experimental animal that follows the addition of glucose to the infusion entering the coronary vessels To produce some measure of the same effect is our hope when we inject small amounts of 50 per cent glucose solution As previously stated large intravenous injections are contraindicated since they increase the blood volume at a time when the heart is already overloaded consequently only small amounts of glucose should be used and all injections should be given slowly I prefer 50 cc of a 50 per cent glucose solution After warming the ampule to body temperature the technic may be simplified by drawing the entire contents into a large syringe and injecting it into an arm vein Five minutes should be allowed to inject 50 cc so that the danger of adding too quickly to the blood volume as well as that of venous thrombosis may be avoided Unfortunately the same effect is not obtained by giving a similar amount of glucose by mouth The excessively sweet solution may cause nausea and slow absorption from the gastro intestinal tract may be expected in the presence of so marked an impairment of the circulation The introduction of a hypertonic glucose solution into the circulation has a vasodilator effect on blood vessels, including the coronaries and this may account for some of the benefit derived from these injections

If respiratory difficulty is present in the form of Cheyne Stokes breathing or paroxysmal dyspnea (cardiac asthma) some improvement may be noted following injections of glucose Caffeine sodium benzoate may be useful in cases of acute occlusion if given intravenously in doses of 7½ grains (0 5 Gm ) every four hours

I have seen two patients (see Figs 243 and 244) develop sudden complete heart block shortly after the onset of an acute coronary occlusion Typical Stokes-Adams seizures occurred in one followed by death six hours later In the other patient these attacks did not occur normal rhythm was re established in two days and the remainder of the convalescence was smooth The management of Stokes Adams seizures is described on page 405

**Ventricular tachycardia** (page 390) may occur following an occlusion and precipitate cardiac failure The attack may end spontaneously but as soon as the diagnosis is established, quinidine sulfate should be given The usual initial dose should be 0 1 Gm (1½ to 2 grains) followed in

two hours by a slightly larger dose 0 2 Gm (3 grains) and later by 0 3 Gm (5 grains) every three hours Quinidine is usually well tolerated by patients suffering from acute occlusion When the attack is terminated it is well to continue 0 3 Gm (5 grains) of quinidine three times daily as a maintenance dose for a period of ten days to two weeks Levine [18] [19] recommends quinidine in 0 2 Gm (3 grains) doses three times a day for two weeks as a prophylactic measure in every case as soon as the diagnosis of coronary occlusion is made hoping in this way that such complications as paroxysmal ventricular tachycardia paroxysmal auricular and ventricular fibrillation may be prevented

Patients with cardiovascular syphilis may occasionally develop acute coronary thrombosis in which event the treatment for the acute episode is the same as outlined above When recovery is complete bismuth and the iodides may be started (page 214)

Complete rest in bed for six weeks is the prescription in all cases of acute occlusion While the practitioners of today are expert in the diagnosis of occlusion many allow their patients to be out of bed before the infarct has had time to heal firmly Willius has demonstrated that in 5 to 22 days after the formation of a coronary infarct connective tissue formation may be recognized and in four to six months the healing is complete The value of careful increase in exercise allowance after the initial six weeks of bed rest is therefore evident if ventricular aneurysms and other complications are to be avoided Useful guides to healing of the infarct are the behavior of the sedimentation rate (page 57) and the subsequent changes in the appearance of the electrocardiogram (page 636) As a rule return to full activity should not be allowed for three months

If at all possible much can be gained by a period of spa treatment at the time when the patient is first permitted to be out of bed (page 513) The education secured here in the matters of diet and activity often proves invaluable The patient learns to be satisfied with life on a much reduced plane which may be an important step toward prevention of recurrence of the episode

A great deal has been written concerning the use of tobacco by patients who have coronary disease Without reviewing the different sides of the question I believe that it is safe to state that enough is definitely known about the effect of tobacco in cases of arterial disease to prohibit its use by patients who are striving to live along with coronary artery disease and avoid its complications

### SURGICAL TREATMENT

Newer treatments have a decided surgical trend Total thyroidectomy has been recommended for coronary disease as well for the complication of congestive failure This procedure has been discussed elsewhere (page 102) More recently Beck[96] has grafted vascularized tissues on the heart in the hope of providing the myocardium with an additional blood supply and relieving the anoxemia Skeletal muscle from the chest wall and fat from

the mediastinal and subcutaneous deposits are the tissues used in this operation A graft from the left pectoralis major is applied to the surface of the heart which is approached from the left side of the sternum At the same time the pericardium is roughened to encourage adhesions between the heart muscle and the pericardial fat that receives some of its blood supply from extracoronary sources Powdered beef bone is used on the surface of the heart in the hope that the inflammatory reaction it produces may increase the number of vascularized adhesions between the graft and the coronary bed Quinidine should be given routinely before and after this operation and the surgeon should be prepared to defibrillate the ventricles if ventricular fibrillation occurs at any step of the procedure (page 475) Patients are placed in oxygen tents for variable periods following operation While Beck s mortality for the first 12 patients was 50 per cent in the next nine cases the mortality was zero So far the clinical results of this procedure are encouraging Improvement in the patient's symptoms is brought about either by the increased blood supply or its more efficient distribution or by interruption at the time of operation of nerve pathways from the heart Final opinion in the matter of the Beck operation will depend upon the clinical course of the first group of patients subjected to the operation when compared to a control series and the size of the collateral channels that will be revealed in the autopsy specimens

At the present writing the physician should continue to treat his patients with coronary disease by the usual medical measures I referred some patients for total thyroid ablation when this procedure reached the peak of its popularity but have so far referred none for the Beck operation In the exceptional case where pain is extreme and cannot be controlled the paravertebral injection of alcohol (page 250) is the *procedure of choice and* is attended by less risk However like the nitrite the medical man administers it is only directed toward relief of a symptom and does not strike at the defect responsible for the disease The Beck operation on the other hand is planned to give the heart muscle more blood If this is accomplished and the mortality remains low our future choice in the matter is obvious

MANAGEMENT OF CARDIAC COMPLICATIONS IN DIABETES MELLITUS

(See page 287)

## ILLUSTRATIVE CASES

### CORONARY DISEASE COMPLICATED BY ANGINA—MARKED IMPROVEMENT FOLLOWING INITIAL ATTACK OF CORONARY THROMBOSIS

**Case 40** G H a city fireman of 46 when first seen on 10/3/33 complained of a crushing chest pain radiating to both arms sudden in onset and increasing in severity Milder attacks of pain similar in type had been present for one month usually appearing when the patient walked up a long hill near his home and disappearing *promptly after* a short rest

The past medical history was negative The family history showed that his *father* and one brother died suddenly of heart disease

PHYSICAL EXAMINATION B P 90/60 T 97 ? P 100 Ashen pallor dyspnea and sweating were noted No cardiac enlargement There was a systolic murmur over the aortic area transmitted to the vessels of the neck The lungs were clear Abdomen negative No edema

DIAGNOSIS A Etiologic Arteriosclerosis B Anatomic No cardiac enlargement Coronary occlusion Coronary infarction C Physiologic Anginal syndrome D Functional Classification Class 4 Therapeutic Classification Class E

Discussion An injection of morphine sulfate 15 mg (¼ grain) was sufficient to give complete relief of pain In two hours the circulatory equilibrium was restored the blood pressure rose to 110/80 the color improved and the dyspnea was no longer in evidence

Complete bed rest for seven weeks was ordered During this entire period the patient s condition was excellent The chest pain did not reappear and the only drug used was phenobarbital which helped on several occasions to allay restlessness and combat insomnia

At the end of seven weeks a gradual increase in activity was prescribed The anginal pain did not reappear Ten weeks after the attack an orthodiagram showed no cardiac enlargement Three months after the attack the patient was allowed to undertake light duties around the firehouse Since there was no return of either chest pain or dyspnea during the next three months a still further increase in his activity was permitted

This patient was examined at regular intervals from 1934 to 1940 He has remained free of all symptoms The heart has not increased in size The electrocardiogram has returned to normal (see Fig 236)

The feature of considerable interest in reviewing this case is the complete disappearance of anginal seizures following an attack of acute coronary thrombosis A tempting explanation is to suppose that the branch of the coronary tree that was responsible for the angina was the seat of more advanced sclerotic changes Occlusion followed by healing that the complete bed rest permitted eliminated this myocardial sector as a focus for pain production The subsequent history of this patient suggests that the remaining coronary arteries if sclerosed are certainly not narrowed to a point where ordinary exertion produces symptoms Due credit must also be allowed for the collateral circulation that took place about this area

The fact that few drugs were employed in the management of this patient deserves comment An initial dose of morphine was given during convalescence an occasional dose of phenobarbital was used and when he returned to work a prescription was written for 2 grain capsules of theophylline ethylene diamine to be taken after meals Nitroglycerine was prescribed and carried at all times but since angina did not reappear it was never used After taking the capsules containing the xanthine derivative for a few weeks the patient was advised to go along without drugs No symptoms reappeared consequently no medication has been necessary during the past few years

A follow up study is now made every three months At each visit an interval history is obtained the heart size checked by roentgen examination and electrocardiographic examination repeated

This patient s record points out that the prognosis in coronary occlusion in some cases is excellent Younger patients tend to do very well if other factors in the history are good The favorable circumstances here include the absence of hypertension and cardiac enlargement and the fact that the anginal seizures did not recur when activities were resumed In addition, the attack itself was readily controlled, recovery prompt pain not prolonged, the fever was not high following the accident and congestive failure and abnormal rhythms did not complicate the picture An unfavorable factor that cannot be overlooked in this case is the poor family history

Many physicians, no doubt, could collect a number of similar instances of recovery following attacks of acute coronary occlusion in which the proper period of bed rest has been obtained and the return to ordinary activities has been gradual Rest undoubtedly is the main feature of the treatment

### Coronary Disease Complicated by Angina and Thrombosis—Improvement Following Careful Regulation

**Case 41** C S an electrical engineer of 53 was first seen in September 1935 complaining of chest pain on exertion for one year In June 1935, an attack of very severe chest pain was experienced lasting three hours and requiring a hypodermic of morphine for relief Bed rest for six weeks was followed by recurrence of anginal pain on slight exertion The patient returned to work two months following the attack but found that activity was considerably curtailed by chest pain

Physical Examination B P 114/70 The heart was enlarged to the left and a soft systolic murmur was heard over the mitral area The heart sounds were normal and the rhythm was regular

The orthodiagram (Fig 112A) showed a slight generalized enlargement The cardiothoracic ratio was 0 57 The transverse diameter was 14 3 cm (predicted 12 8 cm) cardiac area 13 sq cm (predicted 110 sq cm) aorta 3 8 cm

The electrocardiogram (Fig 112B) suggested that the recent severe attack of pain was caused by a coronary occlusion The infarct was thought to involve the anterior part of the left ventricle and the septum

The blood Wassermann was negative The blood count kidney function and concentration tests were all normal

Clinical Diagnosis A Etiologic Arteriosclerosis B Anatomic Cardiac hypertrophy Relative mitral insufficiency C Physiologic Anginal syndrome Normal sinus rhythm D Functional Classification Class 3 Therapeutic Classification Class C

**Discussion** A history of anginal attacks of a year's duration followed by an occlusion and persisting chest pain is not a very encouraging combination The amount of structural damage evident on physical examination that was confirmed by the electrocardiogram and orthodiagram made me hesitate to give this man s family anything but a poor prognosis However let us see what he accomplished

The patient s history revealed that he lived in the suburbs in a three story house on a hill Trips up the hill especially in winter weather were always attended by a great deal of precordial pain His work was difficult and he was constantly under a severe nervous strain In addition there was considerable difference of opinion between the patient and the manager of his department These emotional upsets increased the frequency

of the anginal attacks during the day There was no time allowed for lunch on many working days and consequently a very heavy dinner was the rule in the evening Excess tobacco was consumed at all times cigarettes during the day and cigars at night Later it was brought to light that the patient was active in a country club and held a minor township position both of

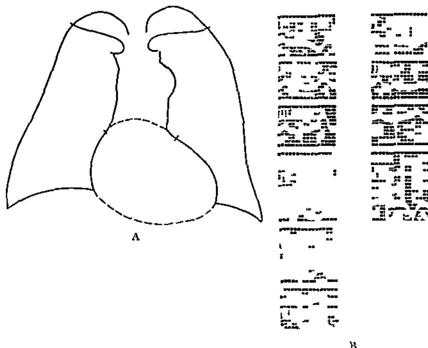



FIG 117 A Orthod a ram Note slight card c enlargement and hypertensive shape Ascend ng ao ta prom nent on r ght border The aortic knob promin nt B Electro card ogram of 6/8/35 shows nverted T 1 with do n ng of the S T interval in the same lead The direct leads (old technic) show bsence of Q aves n leads 4 and 5 and upr ght T waves n same lead The tracing taken on 1 /15/39 shows less marked change Lead 4F ho ever s suggestive Note sharply inverted T ave and the doming of the S T interval

which consumed the greater portion of his spare time in the evenings and on week ends

*The first step toward readjustment of this man s activities was taken* when he moved out of the house on the hill and secured a first floor apartment in the vicinity of the suburban railroad station This eliminated hill climbing in the evening Meanwhile the patient s wife learned to drive a small car and acted as chauffeur on all occasions In fair weather she drove the patient to the door of his office building and in bad weather to the railroad station An hour was taken for a light lunch When oppor tunity presented the patient was transferred to another department in hi

company that gave him a slight reduction in salary but shorter hours, a new department head and eliminated trips on the road

The anginal attacks gradually became less frequent and less severe Instead of 12 to 14 nitroglycerine tablets a day, he found that he needed only two or three Lighter meals were taken at night, and tobacco and coffee were eliminated A longer night's rest was at first made possible by a sedative but later this was withdrawn As soon as possible the patient resigned from his township office and the country club and replaced his golf by developing an interest in book collecting This was a fortunate hobby to choose and many of his evenings and week ends were spent in reading and discussing his books When summer came a two-months vacation was arranged and a bungalow rented at the seashore, where the same program was continued

This patient has now had five years of comparative comfort Anginal attacks have gradually decreased, although when he was last examined (December 15 1939) he reported an average of one or two slight seizures a day He has learned to take a nitroglycerine tablet under the tongue just before undertaking exertion that previously brought him a little above the pain threshold In this way he is increasing his collateral circulation for when the dilator drug opens up the coronaries who can say that the light exercise that follows does not force blood along new pathways?

The interest taken by this patient in getting well and the great help given him by his wife in every detail of his program account for the good result I doubt if any surgical operation directed toward increasing the collateral flow could have given any greater relief than was obtained on the medical regime The last electrocardiogram (see Fig 112B) taken five years after the first still shows evidence of the old infarction in the pronounced inversion of the T-waves in lead 1 The heart size decreased during this period (see Fig 112A)

This case history again illustrates that drugs play a very minor role in the treatment of coronary lesions A carefully planned program given to a patient who has the will to survive often produces a similar result If one of the newer coronary dilator drugs had been given to this man continuously during his course of treatment much undeserved praise would have been given to an agent acting only in the role of a placebo

This patient also demonstrates the need for individual treatment in coronary disease The plan of battle should be drawn up when the full account of each hour of the day is at hand Faith should then not be pinned on a multiplicity of drugs (that are usually changed or rearranged at each office visit), but on the result of the correction of many problems brought to light by a complete understanding of the patient's temperament, occupation and home environment

### Coronary Occlusion (Unsuspected)—Sudden Death Following Rupture of Left Ventricle Through Area of Infarction

**Case 42** W L a white male of 80 wandered into the Philadelphia General Hospital on 11/7/33 He was confused and disoriented but showed a fair state of nutrition




Fig 113 Cardiac rupture through area of infarction on the posterior surface of the left ventricle A Site of rupture behind posterior papillary muscle B Posterior aspect There was an occlusion of the right coronary artery about 2 cm from its orifice The aorta showed advanced sclerotic changes (Autopsy No 8236 Philadelphia General Hospital )

PHYSICAL EXAMINATION The physical examination was normal except for the changes in the eyes and cardiovascular system that are commonly met in senescence There was no cardiac enlargement no arrhythmias were present and no murmurs were heard The heart sounds were weak and distant

LABORATORY DATA The Wassermann was negative the blood count normal and the urine showed only a slight trace of albumin The blood urea was 19 mg per cent

During the following two weeks the patient showed little change in his mental or physical condition On the morning of the 17th hospital day he was found dead in bed

AUTOPSY (Fig 113) The pericardial sac was found to contain 700 cc of bloody fluid and a large blood clot A small mottled rupture was seen on the posterior surface of the left ventricle Heart weight 440 Gms Coronaries prominent tortuous and sclerosed Myocardium mottled and flabby The area toward the apex resembled scar tissue of a healed infarct On opening the heart the site of the rupture was seen behind the posterior papillary muscle There was a small break in the endocardial surface about 5 mm in diameter No clot was attached The mitral and aortic valves were slightly thickened Both coronary orifices were markedly sclerosed especially the left About cm from its orifice the right coronary artery was found to be occluded It contained an adherent dark red clot extending into the two branches for several cm The aorta showed advanced sclerotic changes

Discussion (Dr Martin P Crane*) Of all the types of cardiac involvement discussed so far the one most likely to result in sudden death particularly in a patient of this age is disease of the coronary arteries In the Philadelphia city morgue where more than 2 000 cases of sudden unexplained and violent death are examined annually this group constitutes the largest percentage Coronary occlusion due to atheromatous change in the vessel wall with subsequent narrowing and reduction of the blood supply is the most common finding [33] The formation of a thrombus in such a vessel occurs in a substantial percentage of cases but is by no means discovered as often as diagnosed Embolism involving the coronary mouths is a rare occurrence in our experience although for some unexplained reason this is frequently the diagnosis made by physicians summoned to pronounce death I have seen only one patient in six years in whom such a diagnosis was justifiable This patient a man of 40 years of age had been operated upon for the removal of a large pilonidal cyst, and at autopsy an embolus was demonstrated blocking the mouth of the left coronary artery and protruding slightly into the aorta The coronary vessels otherwise were in excellent condition throughout The diagnosis here incidentally was not made ante mortem

Autopsies performed to investigate the cause of sudden death in cases in the age group of the patient whose history appears above generally show the late results of coronary disease i e single or multiple areas of infarction aneurysmal dilatations of the ventricle or rupture of the myocardium through an area of softening in an infarct The most remarkable feature of many of the individuals presenting extensive lesions is the paucity of symptoms they appear to have exhibited before death according to the histories we obtain from their relatives or associates

Another observation that has interested us is the absolute lack of corre

* Chief Coroner s physician City of Philadelphia

lation between the extent of the infarcted or scarred area and death Many hearts have revealed such massive and obviously long standing lesions that we have wondered many times how the patient was able to survive and carry on strenuous activities in spite of such extensive myocardial damage Many of the infarcts that are encountered are often larger than a silver dollar On the other hand in some cases where death takes place suddenly no infarction may be present or if it is found after a search it may not exceed a ten cent piece in size In these cases we must seek the cause of death in the profound disturbances of cardiac rhythm initiated by this small area in the myocardium

In syphilis of the aorta simple narrowing of the coronary orifices without occlusion may produce sudden death (page 210) In such hearts the condition of the coronary vessels may be quite satisfactory beyond their point of origin in the diseased aorta

Hypertensive cardiovascular disease is in our experience second to coronary disease as a cause of sudden death It is of course frequently associated with coronary artery disease although it may operate as an independent factor in the production of the terminal episode Hypertension and syphilitic aortitis particularly in negroes appear to be a common combination in the production of sudden cardiac failure The enlargement of the left ventricle and the sudden demand for increase in the coronary blood flow in the presence of such a marked narrowing of the mouths of the coronary vessels in the aorta are the factors that explain the terminal episode

The effect of a sudden mental shock in these individuals was well illustrated by two cases observed recently at the city morgue A male negro collapsed and died suddenly while at work on a laboring project His body was brought to the morgue his associates meanwhile going to his home to carry the news to his wife She promptly collapsed and was pronounced dead in a few minutes Her body was likewise removed to the morgue Their hearts were identical in revealing syphilitic aortitis and the effect of long continued hypertension with marked left ventricular hypertrophy They differed only in weight the heart of the husband weighing 650 Gm, and that of the wife 600 Gm

Syphilitic aortic regurgitation and arteriosclerotic aortic stenosis are the chief valvular lesions that are associated with sudden death Rheumatic valvular disease is a distinctly rare cause in our autopsy experience at the morgue While it may occur it is less frequent than either of the two previously mentioned The youth of the patients who develop rheumatic lesions the comparatively little myocardial damage some of them reveal after the active process subsides as well as the wide clinical recognition such valvular lesions enjoy probably account for the fact that we see them so infrequently in our department Congenital lesions such as pulmonary stenosis and its combinations are in my experience rarely the cause of sudden death

Rupture of an aortic aneurysm syphilitic in origin is by far the most

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* Chief Coroner s physician City of Philad lphia

A suitable hypertensive regime was prescribed (page 305) and the patient was given instructions in adjusting his work to the level of his myocardial reserve

When next examined 14 months later all the signs of acute coronary occlusion were present Morphine was given at once for pain Three injections of 15 mg (¼ grain) each were required at two-hour intervals For the dyspnea and cyanosis oxygen was administered through a nasal catheter (page 99) at the rate of five liters per hour It was continued for 36 hours Three injections of 50 cc of 50 per cent glucose were given during the first 24 hours at eight hour intervals The patient showed gradual improvement following these measures and on the seventh day normal rhythm returned spontaneously (see Fig 243C) No digitalis was prescribed The remaining seven weeks of his period of bed rest were uneventful

When slight exertion was allowed at the end of this time a marked increase in the amount of dyspnea was observed His activities were restricted in an attempt to conform to this reduction in myocardial reserve and he was kept on one floor of his home for another month At the beginning of the fourth month the patient insisted on returning to his work as janitor of an office building Although he was advised against undertaking the work incident to this position the patient managed to go along for a year during which time he continuously showed signs of mild congestive failure He was digitalized two months after his attack of coronary thrombosis Intermittent claudication appeared during the first few months following his return to work although anginal pains were never experienced The claudication no doubt was more efficient in limiting his activity than the advice we gave him In addition to the maintenance digitalis tablet of 0 1 Gm (1½ grains) daily theobromine sodium acetate 0 3 Gm (5 grains) was given after meals No improvement in the claudication was noted

Two years after the acute occlusion edema of the feet became marked and persisted The heart showed increase in size and the exercise tolerance showed a further reduction Ordinary activity produced marked dyspnea Weekly injections of mercupurin (2 0 cc ) were given with ammonium chloride 1 0 Gm (15 grains) after meal this regime removed all evidences of edema

Two months later however the patient began to have frequent attacks of nocturnal paroxysmal dyspnea and died suddenly during one of the seizures No autopsy was obtained

Following the posterior coronary occlusion which must have been a large one this patient did not have enough cardiac reserve to carry on without discomfort He was always on the verge of congestive failure Dyspnea was marked on slight exertion and later dyspnea of the paroxysmal nocturnal variety entered the picture Death occurred during one of these sudden episodes of left ventricular failure Reviewing this record it is remarkable

how long the patient was able to survive following first, the acute failure of his coronary circulation, and later, cardiac failure of the congestive type

The most interesting feature of his single attack of coronary thrombosis is the sudden onset of heart block When this occurs the blood supply to the bundle of His has usually been sharply curtailed and momentary cessation of ventricular activity cerebral anoxemia and Adams Stokes seizures are not uncommon sequelae It is strange that this patient never lost consciousness when his pulse fell suddenly to 40 As a rule the greater the degree of bradycardia, the more serious the situation becomes and the more likelihood there is that Adams Stokes seizures will develop The sudden appearance of bradycardia of this degree following the attack of chest pain enables the clinician to make a diagnosis of posterior occlusion and to predict that the lesion is in the right coronary artery The infarct that results usually includes the posterior portion of the interventricular septum and the posterior surface of the left ventricle Since the infarct faces posteriorly, no friction rub is heard

It will be seen (see Fig 243C) that normal rhythm returned later This may be interpreted as evidence of the development of a collateral circulation in the tissues about the bundle On the other hand adequate anastomoses in the septum may prevent the occurrence of heart block when occlusion involves this region

In some instances following an acute coronary occlusion intraventricular or bundle branch block may accompany an A V conduction defect in which event the gravity of the situation is increased [63] [99] While complete heart block complicates coronary occlusion in from 0 7 to 4 0 per cent of the cases,[19] [6] intraventricular block has a much higher incidence Master has reported this finding in 15 per cent of 375 cases As a group these patients are older and present evidence of more advanced cardiac damage

Usually the complete block is permanent (page 406) in fact this arrhythmia may be the only remaining evidence of a previous occlusion when the patient is seen some time later Many of the unexplained prolongations of the P R intervals that are often encountered later in life no doubt represent a more gradual interference with the coronary blood flow Repeated occlusions have a tendency to increase this conduction defect until permanent complete block occurs (see Fig 181)

## Acute Coronary Occlusion Complicated by Complete Heart Block—Death During an Adams Stokes Seizure

**Case 44** W S a railroad engineer of 69 was first seen in April 1934 complaining of vertigo and dyspnea

Physical Examination B P 170/100 There was cardiac enlargement chiefly left ventricular aortic dilatation and an advanced degree of cerebral sclerosis

Laboratory Data The urine showed fixation of the specific gravity The blood Wassermann and blood count were negative

Course On these findings the patient obtained a railroad pension and with increased rest and digitalization showed few circulatory symptoms for a period of five years During this time he was examined three times and the orthodiagram and electrocardiogram showed no significant changes

In August 1939 there was a sudden attack of chest pain accompanied by sweating and signs of shock His course was rapidly down h ll in spite of the usual measures (morphine oxygen and glucose) Twelve hours following the onset of chest pain the pulse suddenly dropped to 45 and dur ng the next six hours he had frequent Adams Stokes seizures in one of w h ch he died (see Fig 44)

**Discussion** Complete heart block following the sudden coronary occlusion in this patient was accompanied by Adams Stokes seizures When these attacks complicate coronary occlusion the outcome is usually fatal The treatment should be directed toward increasing the pulse rate and may be planned accurately only when the cardiac mechanism during the seizure has been determined by an electrocardiogram Epinephrine is safe to use in cases of ventricular standstill but in the presence of coronary disease it should always be used with care Management of Adams Stokes seizures is discussed in detail on page 403

MANAGEMENT OF THE CARDIAC COMPLICATIONS OF DIABETES MELLITUS

In the era before insulin coma acidosis infection and malnutrition were the chief causes of concern Hospital admissions in coma were not uncom mon Today diabetics do not die in coma and in fact are rarely seen in this state They are living longer and in increasing numbers are showing advanced changes in the coronary arteries[177] The chief cause of death in diabetic patients is now arteriosclerotic heart disease Symptoms of coronary disease are much more frequently met in diabetic patients than symptoms arising from arteriosclerotic involvement of the vessels of the brain periph eral arteries or other sections of the body

Many theories have been advanced to explain the close association between arteriosclerosis and diabetes Joslin[176] believes that the increase in blood cholesterol bears a direct relationship to the arterial changes evi dent in both young and old diabetic patients The frequency of the onset of diabetes in later life has suggested to some that the disease is the result of arteriosclerotic involvement of the pancreas which is only a part of the widespread process However postmortem studies that show the high incidence of arteriosclerosis in the young diabetic patient are certainly not in agreement with this view Angina pectoris and coronary occlusion are more common in women with diabetes than in nondiabetic women of the same age group which is further proof of the role of diabetes in the production of these vital changes

There is a greater incidence of arteriosclerosis in poorly treated or neglected cases of diabetes The longer the time before the disease is recog nized or properly managed by diet and insulin the greater the degree of arterial change that will be evident on clinical examination Nathanson[77] has shown that a high degree of vascular disease may be found in the young diabetic who survives for a period of ten years or more In an analysis of 100 autopsies upon diabetics this observer found an incidence of 41 per cent of severe coronary disease Above the age of 50 years the incidence was found to be 51 7 per cent as compared with eight per cent in an even larger series of nondiabetics of the same age

Hypertension is very common in diabetic patients Bell and Clawson[6] state that the incidence of hypertension is five times as great among diabetics as among nondiabetics This in turn has an influence on the degree of arteriosclerotic change in the coronary tree The increase in the blood pressure so common among diabetics cannot be attributed to the arteriosclerosis Obesity is certainly a factor that deserves consideration, as well as the variety of metabolic alterations that accompany diabetes

Many theories have been advanced to explain the development of arteriosclerosis (page 541) Since the majority of cases of diabetes in our country are over 40 an age when sclerotic changes are frequently encountered in nondiabetic patients the problem presented is by no means an easy one Furthermore there are no differences in the fundamental character of the *pathologic change in the two groups of patients Often a high degree of* sclerosis can be demonstrated in young people who have diabetes that has been improperly controlled To explain this, we again come to cholesterol, a substance that no doubt holds the key to the mystery The faulty metabolism that produces high concentration of this substance in the blood may have a direct relationship to the sclerosis The high blood sugar of the diabetic is likewise not a silent chemical abnormality

The effect of the dietary beliefs that characterized the diabetic management during different epochs may provide some important clues in the future in regard to the etiology of arteriosclerosis In the days before insulin the high fat low carbohydrate schedules favored sclerosis High carbohydrate diets combined with proper insulin regulation may be shown in the future to slow the process

Explanations of some of the other aspects of the problem of arteriosclerosis and its association with diabetes are not available For example why the same pathologic change appears to affect one section of the arterial system to a greater degree than another section remains unsolved

Since the important cardiac lesion in diabetes is coronary sclerosis it is not surprising that the incidence of angina pectoris in diabetic patients is high Root and Graybiel[3 1] reported 210 cases of angina from a series of 7 000 cases of diabetes Of these patients 122 were males and 88 females The much higher relative proportion of females in this series emphasizes the importance of diabetes in the etiology Angina may occur in the diabetic patient who has had the disease for some years and it is more common in patients who have had indifferent treatment Consequently when angina appears in young individuals, in addition to searching for evidences of syphilitic infection it is extremely important to think of the possibility of diabetes

The presence of diabetes usually increases the gravity of the prognosis in angina In a series of 136 fatal cases reported by Root and Graybiel the average duration of life from the time of the first attack of angina was two years the majority of deaths (52 5 per cent) occurring during the first year The early detection of diabetes followed by careful treatment is therefore extremely important in the prevention of angina

In some cases marked coronary sclerosis may be present and give no symptoms until occlusion occurs If this possibility is overlooked and attention focused on the diabetes a diagnosis of diabetic coma might possibly be made However an estimation of the blood sugar and an electrocardiogram usually make the differential diagnosis

In the management of the cardiac patient who has well established coronary disease it is extremely important to realize that the diabetes may be much improved by accurate measures whereas the symptoms of coronary disease may grow proportionately worse I have seen serious accidents result from a too rapid reduction in the blood sugar level Over dosage with insulin with the sudden production of hypoglycemia is usually responsible but an extremely low carbohydrate diet may have the same effect In these cases prompt relief may be obtained by supplying the heart muscle with the necessary glucose by the use of intravenous injections of 20 cc of a 50 per cent solution

In the treatment of coronary disease in an elderly diabetic patient, *insulin is not contraindicated It is well to begin with a diet slightly* under the total energy requirements protein 2/3 Gm per kilo carbohydrate 3 Gm per kilo and fat to make up 15 calories per kilo Insulin should be started in very small doses and increased with caution until all sugar disappears from the urine Frequent blood sugar determinations should be made in order that reactions may be avoided A protective dose of 15 Gm of carbohydrate in the form of orange juice two hours after insulin is a great aid in preventing hypoglycemia in the treatment of elderly patients with coronary disease Fear of insulin shock however should not prevent the careful therapeutic use of insulin in this group Overdosage will give untoward effects but this is equally true with regard to many other valuable remedies that we use in daily practice Insulin carelessly given will cause cardiac pain which may be dangerous Insulin cautiously given to the same patient with a properly calculated diet will give great relief

In rare instances of spontaneous hypoglycemia (hyperinsulinism) the predominating symptom in older patients may be chest pain[38] Here the relationship of angina to hunger should serve to arouse the suspicions of the examiner Relief of the attack following the ingestion of sugar in a readily assimilated form is prompt I have seen one patient of this type a woman of 52 who was first treated by a neurologist for ' petit mal At the onset weakness frequent mental lapses and anxiety were prominent symptoms On questioning this patient when she was sent to me because of the additional symptom of precordial pain she stated that one of the nervous habits that she was instructed to overcome was excessive appetite To hide her increasing desire for food she made frequent visits to a neighborhood restaurant when she felt a spell coming on She even provided for emergencies when the restaurant was closed by hiding pound boxes of candy at strategic points about the house The first time I examined the patient I prescribed a reduction diet and nitroglycerine These directions

were quickly changed when further study, in addition to the signs of moderate sclerosis and slight cardiac enlargement, showed a fasting blood sugar of 60 mg per cent

The management of attacks of coronary thrombosis in diabetic patients with the exception of careful dietary regulation and insulin differs in no respect from the regime outlined on page 272 The insulin will usually be found to be insufficient in most cases and will have to be carefully increased If a few days elapse before this higher blood sugar level is discovered no harm results while hypoglycemia produced by careless insulin dosage in these acute cases may be dangerous

Congestive failure while not a common complication in diabetic patients usually causes a rise in the blood sugar and additional insulin must be administered as indicated Treatment of the edema consists in the use of digitalis (page 76) and diuretic drugs A low carbohydrate diet is useful and small frequent feedings should be given (Chapter 21)

### Diabetes Mellitus Complicated by Arteriosclerosis with Angina and Intermittent Claudication

Case 45 M F a Jewish merchant of 44 was first seen November 7 1938 complaining of precordial pain and shortness of breath

History In the fall of 1936 diabetes was first discovered and the patient was placed on a diet with insulin On exertion at this time he complained of pain in the calves of both legs which was relieved by rest Six weeks before the first examination he noticed tightness in his chest on exertion this was also relieved by rest An occasional spell of dyspnea was experienced during the night Recently he had a severe seizure that required a hypodermic of morphine for relief The patient s father had hypertension His mother had diabetes

Physical Examination Height 5 5" weight 200 pounds B P 106/60 Pulse 80 Marked pallor slight dyspnea Heart sounds weak and distant Rhythm regular Slight cardiac enlargement to the left The liver was not palpable Marked sclerosis was evident in peripheral vessels No edema

Laboratory Data Orthodiagram (Fig 114A) shows cardiac enlargement of the hypertensive type The electrocardiogram (Fig 114B) shows T wave changes in all leads the most marked alterations appearing in lead 4F

Diagnosis A Etiologic Diabetes Arteriosclerosis B Anatomic Cardiac enlargement Old coronary infarction Coronary sclerosis C Physiologic Anginal syndrome Paroxysmal cardiac dyspnea D Functional Classification Class 3 Therapeutic Classification Class E

Discussion The family history here is most significant Both the patient s mother and father were overweight In addition his mother had diabetes and his father had hypertension

This patient at 44 showed evidence of advanced arteriosclerosis in eye grounds and in peripheral vessels The cramp like pains in the calves of the legs on walking that were relieved by rest and the characteristic chest pain confirmed the impression of widespread arteriosclerosis

The obesity must be considered an important factor in precipitating the diabetes which may have been present and unrecognized for many years prior to the time he developed intermittent claudication and first visited his physician

The attacks of dyspnea at night point to left ventricular failure secondary to the coronary disease Theophylline ethylene diamine was given in doses

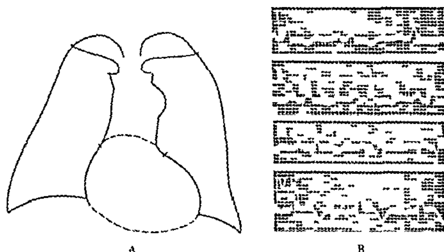



FIG 114 A The orthodiagram Cardiac enlargement is present B The electrocardiogram Marked T wave changes are present in all leads The most characteristic deformity is seen in lead 4F Here there is slight elevation of the RS T interval above the isoelectric line and the T wave is deeply inverted There is a small Q wave in lead 3

of 0 3 Gm (2 grains) after meals and hypodermic injections of morphine for severe nocturnal dyspnea Following the last attack of dyspnea the patient was digitalized

# 9

# HYPERTENSIVE CARDIOVASCULAR DISEASE

Diseases never follow the same pattern even those which are placed in one group There are no more two diseases identical in course than there are two leaves of a plant exactly similar —CORVISART

*Essential hypertension and its complications are problems of everyday* practice Since the hypertensive process once established places a great strain on the circulation many of the complications that arise are related to the cardiovascular system In some patients the duration from onset to heart failure is a short one, others show a great tolerance to the presence of an increased blood pressure over long periods and cardiac symptoms occur late if at all in the course of the disease

The terms employed in the past to designate this type of cardiac disease have been responsible for much confusion Of these chronic myocarditis is one still used by many physicians to designate any type of nonsyphilitic heart disease seen after the age of 40 Although this simplifies their diagnostic problems considerably the use of the term does not give full recognition to the fundamental causes of the heart failure in many of the cases Furthermore the term myocarditis aside from being a bugbear to statisticians is in itself misleading There is no inflammatory process present in the hearts of this group even when examined microscopically If the presence of fibrous tissue is discovered in the myocardium it is by no means proof of a pre existing inflammation since it may be the result of antecedent coronary occlusion with infarction of a large or small area of heart muscle Cardiorenal disease is also an unsatisfactory term to use in referring to cases of cardiac enlargement accompanied by signs of cardiac (rarely renal) failure

Hypertension is merely a symptom However when it becomes established and there is continued elevation of both systolic and diastolic levels of the blood pressure we speak of the condition in the absence of a known cause as essential hypertension This condition we are apt to regard as a disease entity While it is true that its cause or causes are still unknown, recent investigations are clearing the picture and many of the widely scattered facts in literature may be utilized in treatment Consequently an inquiry into the known causes of hypertension seems appropriate at this time

## ETIOLOGY

The classification of Williams and Harrison[400] on page 294 is an excellent etiologic summary

This grouping shows that a variety of clinical conditions may cause elevation of the systolic and diastolic blood pressures

**Among the neurogenic** are included first of all the psychoneurotic group often mistaken clinically for thyrotoxicosis in whom marked fluctuations in blood pressure occur following emotional upsets Other symptoms of neurosis are present and for this reason sedatives like phenobarbital are a great aid in management In other cases following long periods of stress and strain we may observe an increased blood pressure The correction of environmental influence in these instances tends to restore the blood pressure to normal

**The injuries to the brain stem** in the region of the vasomotor center which occur in diphtheria poliomyelitis and encephalitis and are accompanied by high blood pressure levels are included under the medullary form The hypertension in these cases disappears following recovery The association of hypertension with the increased intracranial pressure of skull fractures is well known

Laboratory animals often show increase in blood pressure following reflex stimulation of the carotid sinus and aortic depressor nerves In man elevation of the blood pressure during an attack of angina or following a coronary occlusion may occasionally be the result of a reflex mechanism from the heart Often this elevation will disappear following recovery from an attack of occlusion

**Endocrine Factors** When the action of the various endocrine substances on the circulation and blood pressure became known it was not unusual that the attention of many investigators should turn in this direction for a solution to the riddle of hypertension The suprarenal medulla was investigated and found to secrete a very powerful hormone possessing a constricting action Proof was thought conclusive when hyperplasia of this area was found in some hypertensive individuals and when patients with adenomas of the suprarenal cortex exhibited hypertension However evidence to the contrary soon accumulated for all hypertensive patients did not show change in the region of the suprarenal cortex The theory that hypertension is caused by excess adrenalin secretion has been further exploded by the failure of modern delicate methods to detect adrenalin in amounts in excess of normal in the blood of hypertensive subjects

Pituitary disease may be associated at times with hypertension when there is excessive secretion from the posterior lobe (basophilic adenoma) Here again adequate proof is lacking since attempts to demonstrate excess of this hormone in the circulating blood of hypertensive patients have failed

It is a common observation that vasomotor disturbances occasionally associated with increase in the blood pressure accompany the menopause

TABLE VII

CLASSIFICATION OF HYPERTENSION*

(R[illegible]ted by perm[illegible]on of the a[illegible]th[illegible] and th[illegible] d[illegible]t[illegible] of th[illegible] An[illegible]l of Intern[illegible]l Med[illegible])

I NEUROGENIC

A Psychogenic
  1 Psychoneurotic §
  2 Stress and strain
B Medullary
  1 Diphtheria §
  2 Poliomyelitis §
  3 Encephalitis §
C Increased intracranial pressure §
  1 Carotid sinus †
  2 Aortic depressor nerves †
  3 Ischemic muscle
    a Cardiac
    b Skeletal

II ENDOCRINE

A Pituitary (basophilic hyperplasia—Cushing's syndrome)
B Adrenal
  1 Medullary adrenalin (pheochromocytoma) †
  2 Cortical tumors
C Ovarian
  1 Menopause
  2 Arrhenoblastoma

III RENAL

1 Acute and chronic glomerular nephritis §
2 Obstruction to urine flow §
  (a) Congenital anomalies §
  (b) Ureteral stricture §
  (c) Urethral obstruction
  (d) Pelvic tumors
  (e) Spinal bladder
3 Urinary tract infection
  (a) Pyelitis §
  (b) Pyelonephritis (classical or masked) §
4 Diseases of renal arteries
  (a) Renal atheroma (large and small arteries)
  (b) Arteriolar sclerosis ‡
  (c) Infarcts of kidney
5 Tumors of kidney
  (a) Wilms tumor §
  (b) Other tumors
6 Coarctation of aorta
7 Renal calculi

IV METABOLIC

1 Hypercholesterolemia (renal atheroma ?)
2 Gout (uric acid deposits in kidneys ?)

V CONGESTIVE HEART FAILURE

VI MIXED AND UNCLASSIFIED CALSES OF HYPERTENSION

* Th[illegible]s does [illegible] [illegible] pat[illegible] w[illegible]th [illegible] [illegible]ly
§ These cond[illegible] [illegible] ses [illegible] ated blood p[illegible]es[illegible] [illegible]
† D[illegible]m[illegible]t[illegible]ated [illegible]
‡ Alth[illegible]ugh [illegible]rteriol[illegible] scl[illegible]os[illegible] p[illegible]b[illegible]bly [illegible] by hyp[illegible] [illegible] se [illegible] blood p[illegible]e

However only a small percentage of women develop hypertension at this time and certainly not a greater number than the hereditary tendency to this disease would account for The disturbed relationship between the endocrine glands or the endocrine balance as we like to call it because of the presence of less ovarian secretion at the menopause may explain the pressure increase in these cases The same hypothesis of imbalance may be utilized to account for the association between hyper and hypothyroidism diabetes and hypertension

**Renal Factors** Hypertension may be renal in origin This thought was originally advanced by Richard Bright when he suggested a causal relationship between renal disease and cardiac enlargement Recently the investigations of Goldblatt and his colleagues have again focused attention on the kidney as a cause of essential hypertension These workers began with the premise that hypertension is associated with vascular disease of the kidney The renal circulatory changes they believe are associated with ischemia By using an adjustable clamp they produced constriction of any desired degree of the main renal artery of laboratory animals In 1932 Goldblatt and his associates reported the production of persistent hypertension in dogs for the first time by renal ischemia These results were soon confirmed and studies to determine the mechanism of the production of the hypertension followed Although space is not available to discuss these important contributions in detail[A] the possible mechanisms whereby hypertension can result from renal ischemia will be mentioned

Goldblatt first considers the increase in peripheral vascular resistance that comes about in order to elevate the pressure and improve the blood flow through the ischemic kidney This may be produced by a nervous reflex from the kidney that is effective through the vasomotor apparatus It may al o be induced by the formation of a substance by the ischemic kidney which accumulates in the blood and acts directly on the contractile elements of the arteries or indirectly by first affecting the nervous vasomotor apparatus Such a substance however has not been demonstrated

Nervous Reflex All the experiments of Goldblatt and his co workers that have been performed to date tend to eliminate a nervous reflex from the kidney as the mechanism responsible for increased peripheral resistance On the other hand their published studies point to the likelihood of a humoral mechanism of renal origin as a cause for the increased peripheral vascular resistance that produces the elevation of the blood pressure Whether the substance is secreted or excreted by the ischemic renal parenchyma and how it finds its way into the circulation are unsolved problems

Endocrine Stimulation Increase in blood pressure may also be caused by stimulation of the endocrine glands by the same unknown substance from the i chemic kidney The hypophysis and the adrenal glands have been studied with this thought in mind but the experiments have been inconclusive

1 1 1 1 3 174 1 5 1 6 1 7 1 8 1 9 130 131 13

Renal Humoral Mechanism The present status of his studie on experimental hypertension has been summarized by Goldblatt[1 4]

> it appears to be established *beyond reasonable doubt that* the hypertension which develops after constriction of the main renal arteries or as a result of renal ischemia produced by any method is due to some humoral mechanism of renal origin Evi dence is accumulating to justify the conclusion that the re ults of these studies on animals may be directly applicable to the pathogenesis of both the benign and malignant phases of essential hypertension in man which is associated with the presence of intrarenal or extrarenal vascular or other disease that can pro duce renal i chemia Further knowledge of the pathogenesis and perhaps treatment of this condition will depend upon the establishment of this conclusion

Coarctation of the aorta is included under the renal heading in the classification proposed by *Williams and Harrison* since experimental narrowing of the aorta above the level of the renal arteries is followed by hypertension while constriction below the renal arteries will not produce it The renal origin of many cases of hypertension has undoubtedly been overlooked until recent years The management of these patients now includes a careful renal study, and high percentages of abnormal pyelo- *grams have already been reported*

**The metabolic group** includes patient who have gout w th an increase in the blood uric acid, also those with hypercholesterolemia Even in these gouty individuals urate deposits in the kidneys have been considered in relation to the occurrence of hypertension

**In heart failure** the systolic and diastolic pressures may fall to normal levels or below and improve when the conge tive manifestations fade from the picture However in other cases failure may cause hypertension to appear and improvement is accompan ed by a fall in pre sure These unusual cases are given a separate grouping in the classification

***Mixed or Unclassified*** *Finally it is obvious that in many instances* more than one factor may be operative in the production of the hyper tension while in others no cause whatsoever will be evident after an exhaustive study has been carried out These cases are grouped under the heading of mixed and unclassified causes

### Malignant Hypertension

When the appearance of essential hypertension is followed by rapid changes in all the arterioles of the body we speak of the condition as malignant hypertension This is not a separate disease but merely a variety of essential hypertension that appears in a different pattern It is a leaf of the same plant growing a little more rapidly to wither and die ahead of the others

In malignant hypertension the factor or factors concerned in the hyper-

tensive process operate in such a manner as to speed up the sequence of events The pressures particularly the diastolic seek higher levels at which they are sustained, intracranial pressure rises and the afferent glomerular vessels become constricted The latter change occurs quickly leading to an irreversible narrowing in the vessel wall

### Incidence

**Race** The incidence of hypertension appears to be increasing a fact that we are in the habit of blaming on the tempo of modern existence We know that hypertension is rare among the Chinese and other races in the Far East who lead more tranquil lives and among African negroes in the primitive state On the other hand hypertension is quite common among negroes living in large cities in America occurring more frequently and at an earlier age in them than in members of the white race Diet and manner of living are the factors that are most often invoked to explain this difference

**Age and Sex** Life we like to be told begins at 40 If this is so perhaps it is more than coincidental that hypertension selects the same period of life for its onset in over 80 per cent of the cases Cardiac complications appear about ten years later Hypertension is equally common in both sexes The lighter occupations undertaken by women may explain the greater mortality rate observed among men and the quicker course the disease takes in the male once it is established

**Familial Tendency** Every general practitioner knows that angina and cerebral hemorrhage appear more often in some families than in others and that either may be the final result of a long standing hypertensive process (Fig 115) A characteristic bodily configuration is generally observed Hypertensive or sthenic types of patients are inclined to be obese and have broad deep chests and short thick necks Obesity hypertension and diabetes are closely allied disorders that appear too often in certain families to be explained on any other than hereditary grounds According to the statistics furnished bv different observers from 50 to 70 per cent of all patients who have essential hypertension give a family history of the condition

Susceptibility Is there any way of sorting out in the early years those patients who will eventually show a permanent increase in the blood pressure level? This is obviously an important question and closely allied to treatment for application of protective measures at an early age might reduce the incidence and the complications in the later years In a person predisposed to hypertension we have reason to suspect that the defect lies in part at least in the sympathetic system Environmental stimuli produce changes in the blood pressure more readily in these individuals than in normal persons of the same age Although these variations are at first intermittent if the stimuli that produce them are continuously repeated the changes may become permanent

Test for Susceptibility A very simple test has been suggested to determine the presence of this over reaction of the blood pressure to stimu

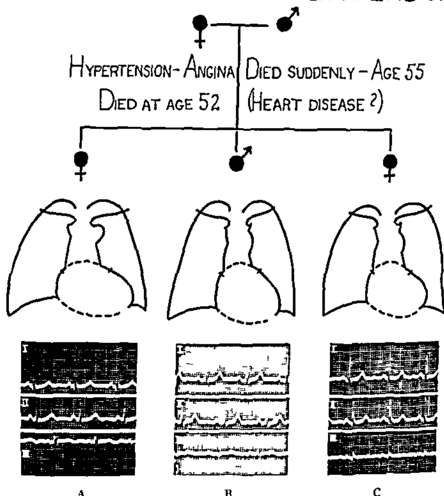



Fig 115 A Housewife of 48 Dyspnea and anginal pain present for two years Over weight B P 210/120 Sclerosis of retinal vessels Marked cardiac enlargement Sys ol murmurs over apex and aortic areas Electrocardiogram (above) shows marked left axis deviation B Mechanic of 45 Slight dyspnea on exertion Overweight B P 180/110 Slight sclerosis of retinal arteries Moderate cardiac enlargement Soft systolic apical murmur Electrocardiogram (above) shows a slight left axis deviation C Housewife of 42 Dyspnea on exertion for two years No other symptoms Overweight Moderate cardiac enlargement No murmurs Electrocardiogram (above) normal B P 170/100

lation If the patient s hand and arm are placed in ice water at 4° to 5 C (39 2° to 41° F), a strong stimulus is produced and the blood pressure

rises In normal patients the elevation in systolic and diastolic pressure will amount to about 10 mm of mercury In patients who are predisposed to hypertension the blood pressure will rise from 30 to 70 mm of mercury This often accounts for the high blood pressure seen when this group of patients is examined for the first time by an insurance company physician In a brief period their pressures return to normal and the finding is usually thought to be of no consequence However if these patients are carefully studied subsequently by the physician the family history of hypertension will be found to be positive in well over 80 per cent of the cases For this reason the careful recording of blood pressure values by life insurance examiners industrial and school physicians in patients who would not ordinarily come under the physician s care becomes a matter of great importance Here early changes may be noted at a time when effective preventive measures may be planned

**Various poisons** have long been mentioned as leading factors in the development of hypertension Lead has been known to exert a vasoconstricting effect on the arteries but it is doubtful if this effect can be a continued one and account for a chronic hypertensive process Tobacco may have some effect on angina and peripheral artery sclerosis but it has not been shown to produce a chronic increase in the blood pressure Alcohol likewise cannot be said to play a significant role in the increase in heart disease at least not through the production of hypertension

Finally about all we can say in regard to the cause of essential hypertension today is that it follows a widespread vasoconstriction of the arterioles of the body cause unknown which increases the work of the heart leading to hypertrophy and eventually to failure A more rapid progression of these changes we refer to as malignant hypertension

## SIGNS

When the chronic vasoconstriction of hypertension becomes established clinically detectable changes in the heart and arteries are not long delayed The late Richard Cabot summed up the situation to his classes briefly The findings in hypertensive heart disease consist of high blood pressure and a big heart Hypertrophy of the left ventricle is first to occur since it is this chamber that feels the strain of the abnormally high peripheral resistance If vasoconstriction continues and increases dilatation of the left side of the heart occurs with widening of the mitral ring and the systolic murmur of relative mitral insufficiency is heard in the region of the apex

**Increase in the pulmonary blood pressure** now follows As the right ventricle receives the strain, it responds in similar fashion by an increase in its size When it can no longer carry the burden it in turn shows dilatation and signs of failure While these changes are taking place in the heart and lungs the aorta is receiving an increased amount of trauma at each systole If viewed under the fluoroscope a widened arch may be noted although this change is not as marked as that observed when

syphilis is present The elevated blood pressure is now reflected in the increase in the pitch of the aortic second sound As the disease advances, degenerative changes appear in the aorta, small tears may occur, caused either by the direct impact of the blood column or by the twisting effect it exerts on the whole arch Later, if these areas give way before the increased force of the blood column dissecting aneurysms may form

Long-continued strain on the peripheral arteries produces a thickening or sclerosis The coronary arteries are so located that they cannot avoid the damaging effects of the column of blood delivered to them under such an increased pressure and all too often rapidly progressive changes in these vessels lead to an early fatal issue particularly if the picture is further complicated by the presence of diabetes

## SYMPTOMS

The patient who has a well established hypertension may have no symptoms whatsoever that would lead him to consult a physician and many times the elevation of the blood pressure is first brought to light by a life insurance examination The course of the disease from this time depends a great deal on the skill of the physician first consulted in explaining the nature of the condition to the patient and on the type of nervous system possessed by the patient who receives this information In some patients a host of symptoms of psychoneurotic nature can be traced back to the day they first learned of the increase in blood pressure To them this figure represents a definite disease and their initial fright prompts them *to travel from physician to physician seeking a magic remedy* for their only complaint 'blood pressure In other patients, from the very onset the hypertensive process may pursue a swift malignant course with wide spread changes and many symptoms that are real, progressive and uncontrollable

**Dyspnea** Between these two extremes there are a number of patients who show structural alterations of a slowly progressing type The first symptoms to appear are usually of a cardiac nature of these increasing dyspnea on exertion is the most common Observing this symptom as the *hypertensive process advances it will be seen to grow gradually worse* and even if the patient is overweight (which is usually the case) the dyspnea may be in excess of the amount noted on the previous examination Dyspnea is the earliest sign of weakness of the left ventricle and if uncontrolled by appropriate measures will progress gradually or rapidly to orthopnea and other evidences of congestive cardiac failure

If failure of the left ventricle occurs quite rapidly in patients with an established hypertension a sudden attack of dyspnea may occur This is known as acute paroxysmal dyspnea or cardiac asthma It comes on *frequently at night when during sleep* the patient slips into an unfavorable position Some cardiac patients may be comfortable in one recumbent position and uncomfortable in another There is a quick awakening with

an increase in the respiratory rate and a sense of suffocation The spell may disappear with change in position or it may become aggravated by the increased respiratory movements which favor a greater venous return to an already overloaded heart Pulmonary congestion increases producing further reflex respiratory stimulation [149] The congestion that follows edema of the lungs places an additional burden on the circulation

Pulmonary edema may come on rapidly during an attack of cardiac asthma Rales appear and these become more numerous and widespread as the spell progresses A frothy blood tinged expectoration often follows an attack in some cases

Cardiac asthma is a common symptom in patients who have had high blood pressure for some time with continued overstrain of the left ventricle The sudden depletion of cardiac reserve following a coronary occlusion may precipitate an episode of this paroxysmal type of dyspnea Cardiac asthma may also complicate the course of chronic nephritis less often it may be secondary to an energetic right ventricle in mitral stenosis suddenly pumping more blood into the lungs than is able to pass the narrowed mitral valve (see Case 15) Too great a volume of fluid intravenously * abdominal distention overactivity cough constipation fright and nightmares as well as faulty posture during sleep are other factors usually blamed for precipitating attacks of paroxysmal dyspnea The relationship between allergy and hypertension is discussed in Chapter 16

**Heart Symptoms** While the continued elevation of the blood pressure causes cardiac failure in most cases intercurrent infections may add the deciding burden that precipitates cardiac breakdown Often when the cause of failure is not apparent clinically an extensive coronary involvement may be discovered at postmortem In some cases anginal pain may have suggested the complication of coronary sclerosis while in others the first intimation of the presence of coronary disease may be a sudden coronary occlusion

Disturbances of cardiac rhythm frequently account for the palpitation complained of in many cases of hypertension Premature beats are common When there is a persisting total irregularity auricular fibrillation is the usual cause Paroxysms of tachycardia or flutter are rare but may occur Advancing coronary disease interfering with the circulation to the bundle may produce varying degrees of heart block

**Nervous symptoms** may precede or accompany these cardiac manifestations and are often so pronounced that they tend to obscure the picture Vertigo headache insomnia tinnitus and inability to concentrate are common complaints of patients who have established hypertension Nose bleeds occur in some instances and may precede a cerebral hemorrhage In hypertension the peripheral circulation may be curtailed to the extent that symptoms are produced in the form of disturbances of sensation (parathesis) or pain on walking (claudication)

* Warning against over-energetic postoperative treatment

Visual symptoms (headaches blurring of vision amaurosis) may appear early in the course of the disease, and the patient will first consult

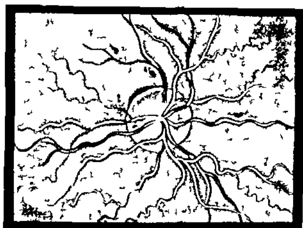


Fig 116 Retinal changes in essential hypertension

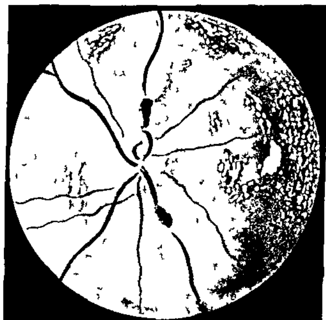


Fig 117 Retinal changes in malignant hypertension

an ophthalmologist at which time the presence of essential hypertension will be revealed by an examination of the visual fields (Fig 116) Experience in the use of the ophthalmoscope is essential in the treatment of hypertension since changes in the eye grounds are common and the

information gained by this examination is useful in diagnosis as well as in prognosis A narrowing of the arteries of the retina which may be the result of constriction or sclerosis is first seen If the change is marked it usually means an advancing lesion Many times the blood pressure of a patient may be normal when examined in which event the retinal arteriosclerosis may be the only evidence on physical examination of a previously existing hypertension

Malignant hypertension also leaves its stamp on the eye grounds in the form of papilledema, retinal lesions and advanced narrowing of the vessels (silver wire arteries) (Fig 117) These changes may be observed far in advance of the renal alterations that characterize the terminal stages of the disease

## DIAGNOSIS

**Cardiac Hypertrophy** It is necessary to demonstrate the presence of cardiac hypertrophy before a diagnosis of hypertensive heart disease can be made This increase in heart size even if the blood pressure happens to be normal at the time should always suggest hypertension in the absence of other causes for enlargement If closely questioned on these occasions the patient will usually give a history of a previous elevation of the blood pressure and often a later reading after circulatory improvement has taken place will show a higher level

**Murmurs and Sounds** In hypertension systolic murmurs are usually heard over the cardiac apex and in the aortic area while the second heart sound in the aortic area is accentuated Rarely when there is a marked degree of aortic dilatation a functional diastolic murmur may be heard in this region I have seen only two cases of functional aortic regurgitation secondary to hypertension Both came to autopsy and syphilitic aortitis was proved to be absent in each instance When left ventricular failure develops during the course of hypertension and the pulmonary circulation becomes engorged the pulmonic second sound may increase until it equals or exceeds the aortic second sound in intensity

If auricular fibrillation is absent a gallop rhythm may also be heard accompanying the failing heart in hypertension (page 15) The third sound that makes up the gallop usually follows the second sound of the heart and is therefore protodiastolic It should be distinguished from the normal third heart sound when the latter is present This is easy as a rule since third heart sounds occur in normal subjects with slow heart rates When a gallop rhythm is heard in patients with hypertension a block of one of the bundle branches should always be suspected The asynchronous contraction of the ventricles that occurs in the presence of this lesion causes splitting of the first heart sound usually best heard between the apex beat and the left sternal border

**Pulsus Alternans** When congestive failure complicates hypertensive

heart disease another sign that should be searched for is pulsus alternans (page 407) for if present, this arrhythmia aids in establishing prognosis Appearance of either pulsus alternans or gallop rhythm in the early stages of failure in hypertensive heart disease is usually indicative of a poor outlook

Other organs in the body that are involved in the hypertensive process may furnish clues that may help to identify the type of cardiac damage if the blood pressure happens to be low when the patient is first examined Kidney lesions may be suspected in the presence of albumin, a low fixed specific gravity casts and nitrogen retention, although these signs if they appear first with the onset of congestive failure, should not be viewed as conclusive evidence of renal damage Transient paralyses, aphasias, as well as headaches point to cerebral changes that may be the result of either angiospasms or cerebral hemorrhages

Hypertension may be said to be present when the systolic blood pressure is persistently above 140 mm of mercury or the diastolic above 90 mm of mercury However many variations occur When first seen the blood pressure in most hypertensive subjects is already established at a higher level the average reading being 170/100 An occasional patient will show a systolic reading as high as 300 mm of mercury Many retain the same blood pressure level for years and feel much worse when attempts are made to lower it In the presence of heart failure or following a coronary occlusion the blood pressure may drop to a normal level or lower The cause of the cardiac hypertrophy is then obscured and the examiner must turn to the history and the physical examination for further evidence Often the diastolic level will not drop to the same extent and will remain well over 100 mm of mercury This is a valuable sign On the whole too much stress is placed on the blood pressure figure itself at the expense of the more significant features of the physical examination

The characteristic alterations in the orthodiagram in hypertension are discussed in Chapter 1 (page 44), and the electrocardiographic changes in Chapter 24

A careful physical examination including the usual laboratory tests will in most cases furnish all the data necessary for a diagnosis of hypertensive heart disease The presence of cardiac enlargement without valvular disease establishes the diagnosis at once in the presence of elevation of the blood pressure If the pressure is not elevated careful attention should be given to the history in order to exclude patients with coronary disease who frequently exhibit cardiac enlargement In these cases the eye grounds may contain the evidence necessary in making the differentiation If the history is atypical and the eye grounds negative it may be most difficult if not impossible to make the distinction without further observation In some cases when congestive failure is successfully treated by appropriate therapy the blood pressure may return to its previous high level, and this observation will often clear the diagnosis

## PROGNOSIS

Accurate prognosis is most essential in this type of heart disease and although there are wide variations a few general rules may be stated Usually the older the patient the better the prognosis since in younger patients the disease is more apt to run a malignant course Patients who first develop hypertension in the fifties or sixties may show few untoward effects

The blood pressure figure itself usually has little significance However if the diastolic pressure remains above 120 there is usually trouble ahead The disease in these cases may take an abrupt malignant course with a quick termination In any event when a diastolic pressure of 120 mm or over is discovered at each examination the duration of life rarely exceeds two years

**Better Prognosis in Women** Women in my experience are able to withstand the effects of a high blood pressure exceedingly well for many years Mild elevations of the systemic pressure that are seen at the time of the menopause may persist and cause little difficulty in later life The course of hypertension in women is less apt to be complicated by coronary accidents

**Complications** Aside from the development of malignant hypertension with its rapidly fatal course complications may at times arise in any case and determine the outcome Congestive cardiac failure is the most common and terminates the disease in over half of the cases Cerebral hemorrhages coronary disease and a progressing kidney lesion in the order named are the next most common terminal events in hypertension Complications therefore arise mainly from the heart and the brain and not as formerly believed from the kidney

The cardiac involvement secondary to hypertension is usually progressive and as a rule the larger the heart the poorer the prognosis Gallop rhythm and pulsus alternans also point to a poor prognosis When attacks of cardiac asthma complicate the picture the duration of life is rarely over a year The presence of angina makes prognosis difficult The patient is always liable to sudden death but with careful management may live a number of years

The assessment of the renal lesion aids in prognosis and in most cases a concentration test will give a good index of renal function If there is fixation of the specific gravity in a young person with hypertension the outlook is grave Older patients may show slower progression of the kidney lesion When uremic symptoms are added to the picture at any age the prognosis is most serious

## TREATMENT

In planning the management of any case of hypertensive heart disease due consideration should always be given to the underlying cause or

causes if they are evident after a thorough physical examination Treatment directed toward the renal endocrine metabolic or neurogenic factors (page 294) whenever possible may lighten the cardiac load and postpone the onset of circulatory symptoms

## Daily Regimen

*If attention is focused on the patient as a whole and his problems* studied in relationship to his environment a therapeutic program may be worked out for each case The object of present-day therapy is not to lower the manometer reading to a figure considered normal for the age of the patient We do not possess any drug or method that we can depend upon to accomplish this permanently The aim in treatment should be to guide the patient in the adoption of a sane mode of living in keeping with his clinical condition This includes suitable exercise, proper dietary instructions, *the prevention of complications and the relief of any annoying symptoms that develop in the course of the disease We should also try* at all times to steer a course away from the many fads of the day If the information is requested the patient should be told the blood pressure level for nothing is to be gained by keeping the matter a secret in a day when patients drift from one physician to another and athletic clubs department stores, and even the boardwalk at seaside resorts have their blood pressure stations

*If there is no cardiac enlargement, particularly in women at the meno-*pause the physician may be justifiably optimistic Likewise in cases of well established hypertension where the patient has progressed well from year to year the records of previous examinations speak for themselves The patient of this type should be told how innocuous an increase in the blood *pressure can be in many instances Proof* can be furnished that it is a condition compatible with old age A great deal of time must be given to explanations following the first complete physical examination, particularly if there are no symptoms present and the physician does not prescribe any medicine

The patient who has hypertension should be educated to meet all situations in his business or in his home with calmness and equanimity and to avoid conflicts as much as possible During recent years few patients *could be advised to seek new jobs Instead they have had to recondition* the old ones to fit a changing physical state Much the same advice can be given to both coronary and hypertensive patients in regard to exercise recreation vacations and other matters of the daily regime

If the patient cooperates in these fundamental matters he may in a very short time feel rested and improved in which event his blood pressure may seek lower levels without the benefit of drugs If drugs had been administered they would have been given credit for in this manner false therapeutic reputations are built by a variety of substances *from carbon*

dioxide to watermelon seeds when enthusiasm lifts them to the realm of cures

Ayman[7] has collected over 200 accounts of procedures and drugs that have been proposed for the treatment of high blood pressure A detailed review of 35 of these showed that all laid claim to either partial or complete success It is evident that the encouragement received with the remedy and the confidence the patient has in the physician go far in bringing the degree of relaxation necessary for symptomatic relief In the early stages of some of the neurogenic types this improvement may be long continued

Buck points out the usefulness of treating cases of hypertension by the methods that have proved their value in the management of the psychoneuroses and recommends similar class instruction This psychologic approach may be useful as a method in large city hospitals for providing the necessary information in regard to diet exercise relaxation and mode of living to large groups who would otherwise receive no instruction in these necessary fundamentals

## Drugs

**Nitrites** Of the various drugs that have been recommended for essential hypertension the nitrites appear to be the first thought of many practitioners Consequently a few words regarding their place in the therapeutic program is in order It is not good therapy to administer one of the nitrite group to be taken at stated intervals as soon as hypertension is diagnosed While it is quite true that the nitrites under some circumstances are excellent in reducing arterial pressure their action is fleeting and frequently if given to patients with advanced arteriosclerosis they produce symptoms that are always annoying and at times may be actually dangerous A sudden lowering of the blood pressure is likely to cause syncope in older people Little is gained because the blood pressure rises again in a short while following the use of the dru and remains elevated until the next dose is taken In the absence of symptoms what benefit could the patient possibly derive from these short periods of blood pressure decline? The use of the nitrite group should therefore be confined to patients with angina pectoris and those showing vasospastic crises and should always be governed by the need of the moment

Nitrites produce vasodilatation because of their direct action on the smooth muscle of the vessel walls They depress systolic pressure to a greater degree than the diastolic and this suggests that their action on the smaller arterioles is less marked A description of the various nitrite preparations in common use will be found on page 247

**Bismuth subnitrate** has recently enjoyed a wide reputation that is chiefly based upon the belief that it is slowly absorbed from the gastrointestinal tract where it supplies a small quantity of nitrite gradually thus sustaining its effect and overcoming this objection to nitrite therapy In

the doses suggested by Stieglitz,[3,6] this remedy has not been successful in my hands

**The iodides** have been advised in small doses in the treatment of essential hypertension and have continued to hold their place through the years Some claim a vasodilating effect follows their use others like their alterative action" The majority of physicians who use the iodides in hypertension find them just as good and not as dangerous as the hundreds of newer remedies whose main action is to depress the blood pressure level When advocates of iodide therapy are overenthusiastic in their claims I always suspect that the hypertension in the patient who shows such striking results is either complicated by syphilis or is secondary to thyrotoxicosis

**Sedatives** are most useful in the treatment of some types of hypertension and have gained a reputation by their action on the accompanying *nervous symptoms They are invaluable in irritable and excitable patients* in securing the rest and relaxation so necessary in successful management In small doses 0 15 to 0 30 Gm (¼ to ½ grain) every four hours phenobarbital will exert a sedative effect rather than a hypnotic one and its administration may be accompanied by a decrease in the blood pressure level Bromides may be continued to advantage combined with the elixir of phenobarbital in some cases Chloral hydrate is a safe and effective sedative and in the usual dosage 1 0 Gm (15 grains) has no untoward effect on the heart

**Endocrine products** have been advocated for the hypertension that accompanies the menopause[7] Here again the effect may not be a direct one since the fall of blood pressure may follow the relief of the annoying symptoms that accompany the condition Other glandular extracts (liver pancreas or thyroid) have as far my experience goes, no definite place in the management of hypertension

**Other Drugs** The remaining host of preparations described in the *numerous pamphlets that increase the bulk of the daily mail* have as far as I know not been proved to be of exceptional value in the management of essential hypertension I mention in passing the sulfocyanates (this group may be actually dangerous) cucurbocitrin benzyl benzoate adenosine adenylic acid acetyl choline and histamine

## Other Measures

**Physiotherapeutic methods** in the treatment of essential hypertension appear to have their greatest value when combined with suitable rest which explains the good reports that follow when they are used as a part of the regular regime of spa treatment Diathermy and carbon dioxide baths are also popular adjuvants at the various resorts (Chapter 19)

**Routine venesection** is not to be encouraged as a beneficial therapeutic measure in hypertension since the blood pressure very quickly returns to its original level when the blood volume is restored However when heart failure comes on with increase in the venous pressure prompt venesection of 500 cc is one of the most efficient methods of restoring cardiac balance

The above measures directed toward relief of the symptoms that commonly arise in the course of essential hypertension constitute the treatment of the patient who has hypertensive heart disease which is asymptomatic If no evidence of congestive failure exists in the absence of auricular fibrillation digitalis should not be given When this drug is needed the presence of hypertension is no contraindication to its use Many times there will be a rise in the blood pressure following the clinical improvement that accompanies digitalization but this should never be regarded as a matter of any consequence On the contrary it shows the ability of the myocardium to restore the blood pressure to the customary level where as the patient has demonstrated greater efficiency may be attained The subjective improvement observed in the patient generally confirms this opinion

**The increasing dyspnea of cardiac failure** calls for prompt and complete digitalization When congestive failure develops in hypertension the measures are the same as those used when failure complicates other types of heart disease These are fully discussed in Chapter 2

**Paroxysmal dyspnea or cardiac asthma** calls for special mention Prevention of the attacks is important and may be possible if attention is paid to the factors mentioned on page 74 A suitable bed (See Fig 38) should be procured whenever possible so that the patient may not run the risk of slipping down into the unfavorable position that initiates a seizure Sedatives should be prescribed to allay nervousness and to secure a full night s rest After recovery from the initial attack the patient should be digitalized This will be found to control or greatly diminish the severity of the seizures for a time in some instances although with increasing weakness of the left ventricle the attacks recur In many of these patients the use of diuretics will again secure some temporary measure of relief Theophylline is useful while the administration of one of the organic mercurial group at regular weekly intervals may be helpful in preventing attacks even in the absence of demonstrable edema (See Case 5) Renal function should be determined before this course of treatment is begun and the existence of a possible obstruction to the urinary flow ruled out In some cases the use of mercurial diuretics in preventing attacks of cardiac asthma in the absence of visible edema may be much more helpful than morphine particularly when vomiting uniformly follows the use of the latter drug Suitable limitation of fluid is necessary in these patients but with routine diuretics this need not be carried to the point where the patient is uncomfortable Care should be taken when diuretics such as mercupurin are used not to insist on too drastic salt restriction A slight readjustment may also be necessary in the daily maintenance dose of digitalis (page 113)

Angina pectoris and coronary occlusion not infrequently complicate the course of hypertensive heart disease Their treatment is discussed in Chapters 7 and 8

The increasing incidence of hypertension its complicating lesions in heart brain and kidney and the futility of most medical efforts to influence its course permanently once established challenge the efforts of all inves

tigators It is natural that the surgeon should become interested in this unsolved problem and not at all surprising that he should choose as his points of attack the endocrine glands and the nerves that carry the constrictor impulses The following brief summary of the surgeon's viewpoint in the treatment of hypertension is furnished by Dr James Lehman

## SURGICAL TREATMENT OF HYPERTENSION

Prior to 1925 the treatment of hypertension was entirely a medical problem Since that time there has been increasing effort on the part of numerous surgeons to perfect an operation for amelioration of the symptoms of high blood pressure These operations have been many and varied In attempts to solve the problem much needless surgery has been done and no doubt is still being done A number of theories have been advanced that attempt to explain the nature of hypertension but so far there has not been a single one that satisfactorily answers all the perplexing problems of management Consequently none of the operative procedure is entirely satisfactory in all cases While time has shown the fallacies of many of the earlier reports concerning operative relief in hypertension too much credence must not be placed in these suggestions no matter how clear and logical they seem It is an encouraging sign that during the past few years some agreement among surgeons has been developing as to the selection of the patient for operation and the type of operation to be performed.

Bitter criticism has been raised in some quarters against the use of surgery for high blood pressure which is after all only a symptom the cause of which is unknown While not denying any of the arguments against surgery much more valid proof has recently been obtained of the usefulness of surgery in arresting the progress of the disease and in producing an amelioration of the subjective symptoms On the other hand it must not be assumed that an operation will ever restore efficiency to an arteriosclerotic kidney nor elasticity to a hardened artery However if cases which are unresponsive to medical treatment are recognized early surgery may find a real place in the therapy of hypertension

No attempt will be made here to review the various operative procedures which have been employed in recent years by both American and European surgeons While there is still no unanimity of opinion the zone of action is narrowing to an area represented by the splanchnic nerves the celiac ganglia and the adrenal glands The operative measures may be classified under three headings (1) adrenalectomy (2) rhizotomy and (3) celiectomy

**Adrenalectomy** Acting on the theory that overactivity of the adrenals was the cause of hypertension many surgeons have practiced adrenalectomy The operation has been more popular in Europe than in this country Encouraged by the reports of cures following the removal of adrenal tumors surgeons wrongly interpreted this form of paroxysmal hypertension with the equally poorly understood essential hypertension Crile

(1916) was probably the first surgeon in this country to perform unilateral adrenalectomy for the relief of hypertension He soon discarded the operation after noting a return of symptoms at the end of one year De Courcy more recently advised bilateral subtotal adrenalectomy and attempted to establish an analogy between hyperthyroidism and hypertension He selects his cases early by tests of renal function and the fundus examination and performs his operations using the retroperitoneal approach through a kidney incision in two stages with an interval of two to three months [77] His statement that it is an accepted fact that hypertension is due to an increased adrenalin content of the blood is not in accord with present-day opinion My experience with this operation while small shows that the results are not permanent and the benefits if any are fleeting

**Rhizotomy** Adson and Heuer have been the chief proponents of rhizotomy They performed section of the anterior roots of the spinal nerves from the sixth thoracic to the second lumbar and found that this procedure was followed by an appreciable drop in pressure in all cases The pressure showed considerable variation with the position of the patient such a drop occurring in the erect position that abdominal support became necessary For this reason rhizotomy has been sharply criticized as a debilitating operation which seriously cripples the patient

Heuer used several criteria in the selection of patients for operation He chose cases where the blood pressure was not fixed and demonstrated this flexibility pre-operatively by making observations (1) after a period of bed rest (2) after the administration of drugs such as amyl nitrite and sodium thiocyanate (3) after the injection of colloidal sulfur or acetyl beta methyl choline The stage of the disease was determined in the usual way by renal function tests by ocular fundus examination and by a cardiac survey Heuer felt that the paralysis of the abdominal muscles was of little significance and was not particularly disabling The best results with this procedure were obtained in cases of malignant hypertension

**Celiectomy or Splanchnicectomy** Today the best results in the surgical treatment of hypertension follow one or both of these operations which are similar in theory as well as in technic The nerves may be severed either above or below the diaphragm Peet uses the intrathoracic approach resects a small portion of the eleventh rib on each side retracts the pleura and sections the splanchnic nerves The lower most portion of the ganglionated sympathetic chain is also removed along with the rami communications from the tenth eleventh *and twelfth intercostal nerves*

Peet places great reliance upon the experimental work of Goldblatt and his associates and believes that in many of the cases he has operated upon hypertension is due to ischemia of the kidneys from overstimulation of the vasoconstrictors of the blood vessels that supply these organs He believes that his operation removes the nervous clamp from the kidneys and recommends the usual criteria in the selection of cases for surgery He also believes that a good result is possible in patients under 50 years

of age whose kidney function tests are still fairly good where ocular changes are not too far advanced, and in whom medical treatment has been tried with no appreciable improvement Some of his cases have shown amelioration of symptoms for as long as five years and most of his patients have obtained symptomatic relief

At the Mayo Clinic, the operation that is favored at the present time by Adson and his colleagues consists in bilateral section of the splanchnic nerves the upper two lumbar ganglia and the intervening sympathetic chain The subdiaphragmatic retroperitoneal approach is used

These workers are in accord with Peet in proposing the neurogenic origin of hypertension Overactivity of the vasoconstrictors they theorize is the cause of the symptoms, and their operation is performed to denervate completely the splanchnic vessels the kidneys and adrenal glands

In the careful selection of patients for operation many tests are per formed pre operatively Their observations show that many of the cases which seem best suited for operation give the poorest results postoperatively *There are also certain sequelae of this operation caused by the removal* of the lumbar ganglia i e loss of sweating in the lower extremities and increased skin temperature that should be noted The male usually becomes sterile however without the loss of libido There is no change in the menses of the female nor in the child bearing function

After a long period of experimentation Crile has evolved the operation of celiectomy Beginning many years ago with unilateral adrenalectomy he changed later to bilateral adrenal denervation while he now performs bilateral celiac ganglionectomy and denervation of the aortic plexus

Based upon comparative anatomic studies, Crile states that

> of highest significance is the role of the celiac ganglia and the celiac and the aortic plexuses which are related to the control of the speed of the circulation of the blood The control of the speed of the circulation of the blood includes the power to raise the blood pressure instantly It includes the quick control of the capillary bed control of the force of the heart beat In other words since the celiac ganglia the celiac and the aortic plexuses the splanchnic nerves and the sympathetic ganglia in the adrenal medulla are the exclusive mechanisms for normal adaptive con trol of the blood pressure and the blood circulation one would logically expect these to be the sole mechanisms which under pathologic activity would raise the blood pressure day and night for months and years until the kidneys the heart and blood vessels and the brain are injured that is are so changed that heart failure brain hemorrhage or kidney failure follow

He therefore concludes

> that celiac ganglionectomy and denervation of the aorta and of the adrenal gland could permanently affect only the physiologic

aspects of the disease and could not affect pathologic changes in the wall of the arterial tree and that in cases that have passed



Fig 118 Incision for celiac ganglionectomy

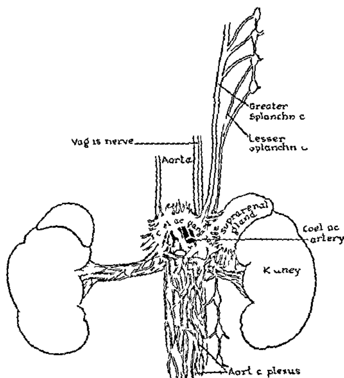



Fig 119 The left celiac ganglion and its connections

the limit of cure the progress of the disease may be slowed down or arrested Since a free plexus of nerves connects the celiac ganglia the adrenal medulla and the entire sympathetic net

work of the body there may be an overflow stimulation to the thyroid gland the pancreas the liver so that a group of symptoms—nervousness palpitation sweating, headache—are produced that is there results a general sympathetic drive These widespread and frequently distressing subjective symptoms are uniformly relieved by celiac ganglionectomy

Crile performs his operation under light gas anesthesia He uses the retroperitoneal approach through a lumbar incision (Fig 118) The celiac ganglion (Fig 119) is located by the sense of touch and dissection is carried out by the trained hand Visualization of the anatomy is not attempted In over 300 cases Crile reports some relief in 87 per cent and complete relief in 35 per cent one year after operation The diastolic pressure was reduced to normal in 39 per cent of the cases [7]

## ILLUSTRATIVE CASES

### Essential Hypertension of Long Duration in Spite of an Overabundance of Unnecessary Treatment

**Case 46** Mrs K K housewife was first examined in January 19 0 at the age of 68 There were no symptoms The blood pressure was 0/100 at that time During the following 0 years the systolic pressure varied from 180 to 30 and the diastolic from 90 to 100 An occasional headache one syncopal attack and vertigo all directly related to medication were the only complaints The exercise tolerance was never impaired and the mental status was excellent

The heart was not enlarged the rhythm always regular and the rate between 60 and 70 A systolic murmur was present over the entire precordium The electrocardiogram showed only a left axis deviation A slight trace of albumin was constantly present in the urine with an occasional hyaline cast Concentration tests showed a specific gravity of 1 016 to 1 0 Death occurred suddenly following cerebral hemorrhage at the age of 88 No autopsy

**Discussion** This patient a relative, was one of the first cases to come under my care She continued to carry out all my instructions and to take the multiplicity of remedies that were prescribed with a degree of faith that I have seldom seen equalled Reviewing my record of her case in the light of modern knowledge of the subject of hypertension, I marvel at her ability to weather trials of all the preparations administered in increasing numbers during these years

Going back 20 years to the time when all attention was focused on the manometer reading I first tried my skill at lowering this patient s blood pressure to a figure that I thought would be a more tolerable level for a woman of her age For the first therapeutic thrust I chose a potent weapon nitroglycerine A few minutes after she took the first triturate (1/100 grain) I received an emergency call to her side Vertigo and syncope had occurred and these were alarming symptoms in an elderly person who had had few complaints in the days before I attended her The blood pressure reading showed that there was no doubt about the fact that my remedy had the desired effect in lowering the blood pressure level How

ever in the presence of arteriosclerosis the sudden insufficiency of the cerebral circulation that resulted produced symptoms and as I was told symptoms had never been present before This was the last time that I prescribed nitroglycerine to be taken routinely by the patient whose only departure from the normal standards of health was revealed by a blood-pressure reading While the quickly acting members of the nitrite group are most valuable for the anginal seizures or the transient cerebral vascular spasms or crises that accompany hypertension they are harmful if given routinely in haphazard fashion

When this patient recovered from her syncopal attack and the first contact she had ever had with whiskey * I fell back on the iodides in order to secure more time to map out a different plan of attack on her blood pressure which (fortunately) at this point had completely regained its former level of efficiency

During the next few months although the blood pressure showed little change the patient was quite certain that she felt much better—at least much better than when she took the last medicine A few months later she was disturbed by many colds in the head and eruptions of the skin It looked like the end for the iodides but by this time elaborate plans had been formulated Sedative treatment could be given to allay the nervousness and lower the blood pressure consequently a sodium bromide phenobarbital mixture was prescribed after meals

A few months later the patient s family complained that Mamma is drowsy and queer A follow up visit at this time revealed an element of truth in both assertions The patient was in bed and examination showed lack of ability to concentrate a slow and indistinct speech and a desire to sleep at all times Although small doses of both sodium bromide and phenobarbital had been prescribed often in older people untoward symp toms may appear They are generally caused by the accumulation of the drugs in the body that follows faulty elimination by an arteriosclerotic kidney All symptoms promptly disappeared when the sedative mixture was discontinued

During the next few years this trusting patient accompanied me through the mistletoe days the benzyl benzoate outbreak the watermelon seed epoch and even cautiously sampled the thiocyanates While she had many more annoying symptoms than were formerly present was it not also true that the years were passing? She was now 80 years of age and should expect a few bad days now and then

A review of the findings at this advanced age showed a blood pressure that was still holding its former level of 220/100 no change in the heart size or the electrocardiogram and no symptoms other than those explain able on the basis of the remedies administered Profiting by this experience it was suggested to the patient that she continue without medicine at least for a time unless symptoms developed This was not a reasonable sug gestion to a patient of her age who had been raised on the belief that

* Formerly pop l r as first aid mea ure in all emergencies especially card c

medicine of some kind is indicated if any abnormality whatsoever is discovered by the physician 'For every disease there must be a remedy' Consequently my last therapeutic *sortie* in her case was a prescription for capsules of appropriate size containing milk sugar They were given with assurance and confidence and were accepted as representative of all the therapeutic knowledge of the day in the matter of hypertension * Immediate subjective improvement followed their use and the patient's statement that she had not felt so well in years I had no reason to doubt for in my own family circle at least I had come of age in the management of uncomplicated essential hypertension

### Hypertensive Cardiovascular Disease Complicated by Congestive Cardiac Failure—Autopsy

Case 47 P C a colored laborer of 42 was admitted to the Philadelphia General Hospital on 5/ 4/36 complaining of shortness of breath and cough

History For the past few years dyspnea had been increasing in severity Six months prior to admission severe attacks of dyspnea had been present at night These were occasionally followed by a blood tinged expectoration Edema was noted a month before admission increasing gradually No precordial pain had been present at any time Chancre in 1909 and antisyphilitic treatment in the out patient department from 1929 to 1936 No history of rheumatic fever

Physical Examination B P 140/105 Marked dyspnea and distention of the neck veins present Heart enlarged to the left as far as the anterior axillary line A musical systolic murmur was heard over the entire precordium with its greatest intensity at the apex A systolic murmur was heard over the aortic area The rhythm was interrupted by occasional premature contractions There were rales at both lung bases Shifting dulness was discovered in the abdomen and the liver edge was palpable below the right costal margin (Fig 120A)

Laboratory Data Urine (24 hour specimen) specific gravity 1 011 trace of albumin Blood count hemoglobin 70 per cent (Sahli) R B C 3 400 000, W B C 13 200 Kahn negative

*Roentgenogram* decompensating (rheumatic) heart disease with pulmonary congestion

*Electrocardiogram* (Fig 120B) Occasional premature contractions low voltage QRS flat T waves and left axis deviation (myocardial disease)

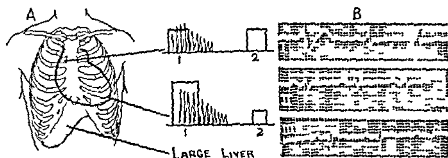
Course During the next two and one half months the patient continued to lose ground rapidly Gallop rhythm was present two weeks before death Attacks of paroxysmal nocturnal dyspnea increased in frequency and the patient died in one of the seizures on 8/7/36

Clinical Diagnosis A Etiologic Hypertension B Anatomic Cardiac hypertrophy Relative mitral insufficiency C Physiologic Paroxysmal cardiac dyspnea D Functional Classification Class 4 Therapeutic Classification Class F

Autopsy (Fig 120C) Heart weight 700 Gm Scattered throughout the left ventricle and auricular myocardium were numerous white scars about 4 mm in diameter with marked thinning of the myocardial wall at these points The valves were normal and the coronary ostia fully patent The aorta showed a few atheromatous plaque but beginning 4 cm above the aortic root were numerous small linear and stellate depressed intimal scar

**Discussion** The increase in the dyspnea over the course of a few years prior to death indicated a gradual diminution in the myocardial reserve Six months before admission the occurrence of attacks of paroxysmal nocturnal dyspnea gave evidence that the situation was becoming an acute one

* *As indeed they were considering her physical findings*




C

Fig 1 0 A Diagram of physical findings B The electrocardiogram Occasional premature beats of ventricular origin (first beat lead 1) The QRS voltage is low all leads The T waves are flat Left axis deviation C Hypertensive cardiovascular disease Cardiac hypertrophy and dilatation A few atheromatous plaques may be seen in the first part of the aorta (Autopsy No 31,914 Philadelphia General Hospital)

With the onset of congestion, the blood pressure dropped to 140/105 If the past history of the patient had not been known, some difficulty might have been encountered at this point in establishing the diagnosis of hypertensive cardiovascular disease The age and the murmurs may have suggested rheumatic heart disease and the history of syphilis in a negro who showed evidence of heart failure may have caused luetic heart disease to be considered as the etiology However there was no history of rheumatic infection signs of mitral stenosis were absent and the rhythm was regular We know that the patient had syphilis for which he received prolonged and satisfactory treatment It seemed unlikely that heart failure could be caused by syphilis in the face of this and in the absence of aortic regurgitation to explain the large heart

The most suggestive sign was the level of the diastolic pressure on admission even though the systolic level had dropped sufficiently to confuse the picture The evidence of the previous existence of hypertension remained in the eye grounds and was reflected in the size of the heart The murmurs could be explained also on the basis of relative mitral insufficiency following the increase in the size of the left ventricle and aortic dilatation secondary to the hypertensive process

At autopsy the definite history of syphilis and the prolonged and adequate treatment that the patient had received over the course of some years led us to examine the first part of the aorta with care There were only a few small healed scars visible in this region These were considered to be unimportant clinically since they neither interfered with valvular function nor caused blockage of the coronary arteries The value of antisyphilitic therapy in the prevention of the progress of aortitis is reflected in this instance (Fig 120C)

When this patient entered the hospital he was given a hypodermic injection of morphine and quickly digitalized He received 0 2 Gm (3 grains) of theophylline ethylene diamine after meals At the end of the first week thoracentesis on the right side yielded 900 cc of fluid During one of the episodes of left ventricular failure that was attended by cyanosis and engorgement of the jugular veins a venesection was performed and 500 cc of blood removed

## Malignant Hypertension in a Girl of 21—Failure of Medical Regime

**Case 48** Miss H M a single American clerk of 21 was first examined in September 1934 The presence of hypertension had been noted a year before when she had a headache of three days duration Since that time headaches recurred so frequently that six months later she was forced to give up her job Lately vomiting accompanied the headaches and she lost 15 pounds in weight The headaches usually were present in the morning and grew worse during the day For a month before examination she had noticed progressing weakness vertigo blurring of vision and palpitation The patient's father died of a stroke at 50 Her mother at 40 had essential hypertension

Physical Examination B P 40/130 Underweight A slight exophthalmus was present The skin was pale and dry No thyroid enlargement The eye grounds showed hyperemia and edema of both discs Large hemorrhagic areas were present on both

retina a w ll a l r f th retinal art r s Th h art ho ed slight enlargem nt to th l ft an l th aortic on l un l s accentuate l

LABORATORY DATA Bl od count was normal th Wassermann negative Blood urea 7 mg per 100 cc The urine sho ed a trace of albumin and the phenophthalein el mination n two hours was normal

CLINICAL DIAGNOSIS A Etiolog c Hypertension (mal gnant) B Anatomic Cardiac enlargement C Phys olog c Normal sinus rhythm D Funct onal Classification Class I Therapeut c Classification Class D

COURSE Rapidly down hill The headaches increased the renal lesion became apparent and the patient following a series of convulsions and a short period of coma died seven months later in the Philadelphia General Hospital

**Discussion** The diagnosis of essential hypertension usually presents no difficulty However the distinction between malignant hypertension and chronic nephritis usually requires a longer period of study

In this patient the absence of anemia the extremely high level of both systolic and diastolic pressure and the relatively good renal function present when first seen were all points favoring the diagnosis of malignant hypertension The picture presented by the eye grounds was likewise suggestive There were no snow banks hyperemia of the disc was present in contrast to the anemia generally seen in nephritis and the retinal arteries reflected the changes that most commonly accompany hypertension

Younger patients are more apt to develop malignant hypertension Instances of this condition are reported in the literature before the age of puberty although this patient is the youngest that I have seen

The onset of the malignant phase of hypertension in this instance was typical Severe headaches usually call attention to the eyes and the discovery of the advanced changes in retina and disc on ophthalmoscopic examination clinches the diagnosis

The extremely high systolic and diastolic pressures in these cases and the edema evident in the discs are signs that suggest the origin of the severe headaches Edema of the brain and increase in intracranial pressure are thought to follow the inability of the arterioles in this region to constrict to the same degree as is shown by similar vessels in other parts of the body The persisting elevation of the diastolic pressure likewise speeds the changes that usually are observed to follow a long continued hypertension and the damage to the arterioles of the kidneys may be quickly reflected in the clinical picture Stupor convulsions and eventually uremia develop in a very short time

The medical management of the complications of malignant hypertension is difficult and the relief obtained usually temporary The patient whose course is as rapid as the one presented here is always best treated in the hospital

Relief of the headache and vomiting is usually the first indication on admission When the blood count is normal the effect of venesection should be tried first In some cases this procedure may bring considerable initial relief of the headache When the symptom recurs the therapy should be directed toward the fundamental cause of the condition The edema of the

brain and increased intracranial pressure may be favorably influenced by intravenous injection of hypertonic sugar solutions Glucose (1200 cc of a 50 per cent solution) may be used but is apt to be followed by a secondary rise in pressure with recurrence of symptoms since it can diffuse into the brain and spinal canal Lately sucrose has been employed in the same concentration and amount and generally proves much more efficient sinc its administration is not attended by a secondary rise in intracranial pressure

Spinal puncture is a useful measure at times in the relief of the symptoms of hypertensive encephalopathy It should be done with care and judgment preferably in the hospital If the initial pressure is found to be high after the needle enters the spinal canal a slow withdrawal of sufficient cerebrospinal fluid is indicated to lower the pressure to normal Spinal tap however is attended by some degree of risk in these cases and the degree of relief it brings to the symptoms is by no means constant

Blackfan and Hamilton [9] have successfully used magnesium sulfate in treating the complications of vomiting and convulsions in these cases For the headache of malignant hypertension it is given by mouth or rectum (50 cc of a 50 per cent solution), or if convulsions develop, it can be administered intravenously (10 cc of a 2 per cent solution per kilo of body weight) The action of the magnesium sulfate when given by mouth or by rectum is brought about by dehydration The action when injected intravenously (or intramuscularly) depends upon the effect of the element magnesium upon the central nervous system Excitability is abolished because of paralysis of motor nerve endings

Sweating has no beneficial action on the cerebral symptoms of malignant hypertension and is no longer advised In some cases it may even be harmful

The nitrites are inefficient and powerless in combating a process of such severity as malignant hypertension, and usually show no appreciable effect on either the blood pressure or the symptoms

### Early Malignant Hypertension—Bilateral Celiac Ganglionectomy

**Case 49** R C a chauffeur of 9 when first examined in December 1938 complained of high blood pressure and nervousness

History Hypertension was discovered two year before first examination Considerable initial improvement followed a medical regime but during the following six months although able to work he felt very much worse Vertigo headaches biliousness and finally dyspnea and palpitation developed He lost ten pounds in weight

Physical Examination B P 240/130 Ophthalmoscopic examination revealed marked tortuosity and narrowing of retinal arterioles and a few scattered hemorrhages on the left retina Both optic discs were hazy The heart showed slight enlargement to the left There was a systolic murmur heard over the mitral area and the aortic second sound was accentuated

Laboratory Data Basal metabolic rate minus ten per cent Blood count normal Blood urea 38 mg per 100 cc Urine showed a light cloud of albumin and hyaline casts

Electrocardiogram (Fig 121A) showed inversion of T waves in lead 1

Clinical Diagnosis A Etiologic Hypertension (Malignant) B Anatomic Cardiac

enlargement Relative mitral insufficiency C Physiologic Normal sinus rhythm D Functional Classification Class I Therapeutic Classification Class C

COURSE Celiac ganglionectomies were performed on January 15 1939 and February 5 1939

DISCUSSION The problem presented by hypertension is indeed a grave one when we consider that 23 per cent of all deaths of persons over 50 are directly attributed to it * The internist has no specific therapy to offer in the management of this condition At the present time he meets the indi

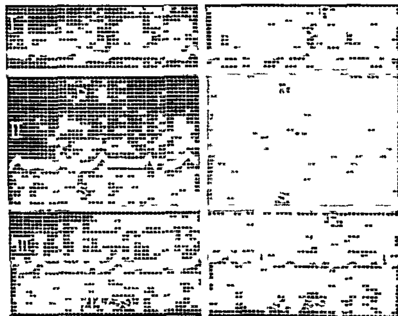


FIG 1 1 The electrocardiogram taken before operation (1/14/39) shows diphasic $T_1$ Following operation (3/11/39) the T wave in lead 1 returned to normal

cations as they arise and treats his patient by the use of carefully planned regimes the details of which have been previously outlined In many cases medical treatment meets all requirements However when the onset of a malignant course is evident surgical measures should be considered for in the presence of these rapidly progressing changes the medical man possesses no therapeutic weapon of value The surgeon on the other hand by his attack on the sympathetic nerve pathways reduces arterial tone at least in part of the vascular tree and in malignant hypertension has so far obtained results that are without parallel in medical treatment

Following operation the blood pressure of this patient was not restored to a normal level Before operation the average readings were 240/120 while during the first year after operation the average pressure was

* Four times the cancer death rate

160/100 However the subjective relief was marked and for this reason he was able to return to work He had few headaches less nervousness, and less exhaustion at the end of the day Furthermore, this improvement in his condition was reflected in the ocular fundi The spasm of vessels was less, and the retinitis disappeared The discs cleared The heart showed a decrease in size, and the T waves of the electrocardiogram became upright (Fig 121B) The albumin was less six months after operation and a decided improvement in renal function was noted

Before operation a marked response in the blood pressure followed immersion of the hand in ice water (page 298) After ganglionectomy this response was less marked but still in excess of normal

While we must admit that perfection in the treatment of hypertension must await further studies the relief that it is possible to bring to properly selected cases by the use of the surgical methods at our command today cannot be overlooked Haphazard surgery in poorly selected cases that have not first been given the full benefit of a medical regime of treatment tends to discredit all operative measures This is unfortunate when we consider that the surgeons have constructed their procedures along lines that conform to all the present-day concepts on the subject of hypertension

## DISSECTING ANEURYSM OF THE AORTA

A rare yet important lesion that may complicate hypertension is partial rupture of the wall of the aorta with dissection of it coats known as dissecting aneurysm Four times (that I am aware of) this accident has occurred in patients under my care In three of these cases that came to autopsy the diagnosis was missed while the fourth was diagnosed correctly If in any type of heart disease all possible happenings are constantly kept in mind there is less likelihood of a diagnostic error consequently it is worth while to review the outstanding clinical features of this unusual accident

Dissecting aneurysm occurs more frequently in males between 40 and 60 years of age who usually give a history of hypertension The first tear in the aorta is most often a transverse one just above the aortic valve through which the column of blood finds its way to the medial coat where it begins to dissect the vessel along the pathway of least resistance It may re enter the aorta at a lower point with the formation of a new channel of variable length (double barrel aorta) or it may extend down to the bifurcation and cause compression of the iliacs Half of the circumference of the aorta may be split to form this new channel and any arteries arising from the vessel along the course of the dissection may be involved Occasionally the dissection travels toward the aortic orifice in which event the coronary arteries are in danger of compression If perforation take place through the adventitia sudden death follows with the escape of blood into the pericardial sac the pleural cavity or the abdomen

Dissecting aneurysm very rarely complicates syphilitic aortitis occasionally takes its origin at the site of an atheromatous ulcer but most frequently selects a spot where a previous medial degeneration has occurred The exact nature of this medial change that Erdheim has designated medionecrosis aortae idiopathica cystica is unknown Some claim that it is merely a degenerative process of old age while others state that it is infectious in origin

## SYMPTOMS

The symptoms attending dissecting aneurysm are sudden in onset and characteristic of the condition Pain is always present It is excruciating and persistent in spite of large doses of morphine Some patients describe it as a tearing pain Usually it is so severe and attended by so profound a degree of shock that consciousness is quickly lost The pain usually centers about the front or back of the chest but in some instances it may be felt in the abdomen in which event the condition is quite often mistaken for the surgical emergency of perforation or embolism (page 483)

The direction taken by the dissecting column often determines the symptoms (see Fig 157) Pressure on the coronary vessels may cause pain that cannot be distinguished from that of occlusion leakage into the mediastinum may produce hoarseness pressure on the renal arteries anuria while compression in the region of the iliac vessels gives rise to symptoms in the extremities Dyspnea is generally present A previous history of hypertension is nearly always obtainable in fact in spite of the shock and collapse the blood pressure may be maintained at a high level The pulse rate varies but is generally increased at the time of the rupture becoming more rapid until it is imperceptible in the presence of internal hemorrhage

Usually death is sudden The longest survival after the onset of pain in the cases I have observed was 48 hours Longer periods have been reported in a recent excellent summary of 19 cases of dissecting aneurysm by Glendy Castleman and White [117] One of their patients lived for 105 days after the formation of the dissecting aneurysm and died suddenly 12 hours after its rupture

The roentgen ray examination may suggest the diagnosis In one case (see Fig 32) the roentgen ray study made on different days revealed a shadow in the left chest following the accumulation of blood in the pleural cavity An increase in the prominence of the aortic knob may occur in other cases following the accident

The electrocardiogram is valuable in ruling out the diagnosis of coronary occlusion It will be negative unless blood flow through either coronary artery is blocked by the dissecting column of blood

Coronary occlusion is the usual diagnosis made in these patients because of the sudden onset the severe pain and (if the patient survives) the subsequent fever and leukocytosis Aside from the electrocardiogram the

points in the differential diagnosis favoring dissecting aneurysm are (1) the tendency of the blood pressure to remain elevated in the presence of so serious a catastrophe (2) the excruciating pain which reaches its peak at once (3) the more widespread radiation of the pain (4) the development of symptoms suggesting obstruction of the circulation at distant points and (5) the absence of a previous history of anginal seizures

*Embolism must be considered in the differential diagnosis* The severity of the pain and the absence of any condition that might serve as a prob able site of origin for an embolus are important points in drawing this distinction

## TREATMENT

Morphine and rest constitute the only therapeutic measures of value when the presence of this condition is suspected All unnecessary move ments are to be avoided in order to delay final rupture of the aneurysm through the adventitial layer If the rupture occurs back into the aortic lumen with the formation of a double aorta long survival may be possible in some instances The importance of rest in these rare cases until healing takes place is evident

## ILLUSTRATIVE CASES

### Hypertensive Cardiovascular Disease—Dissecting Aneurysm—Autopsy

**Case °0** A R a colored laborer of 44 was admitted to the Philadelphia General Hospital complaining of severe pain in the chest and abdomen

History The patient was well until a week before admission when he suddenly developed vertigo which was followed at once by a severe plitting pain in the abdomen and chest lasting several hours His right leg be ame numb following the seizure A few days later there was recurrence of pain and the patient was admitted to the hospital

Physical Examination Well nourished negro slight dyspnea BP 190/130 Advanced arteriosclerotic changes in both fundi Heart slightly enlarged to the left The area of supracardiac dulness was increased There were systolic murmurs over the aortic and mitral areas Epigastric tenderness

Laboratory Data Wassermann negative W B C 16 000 The urine showed a light cloud of albumin but no casts

Course On the second hospital day the patient complained of severe chest and abdominal pain and died suddenly

Clinical Diagnosis A Etiologic Hypertension B Anatomic Di ecting aneurysm Slight cardiac enlargement C Physiologic Normal s nus rhythm D Functional Classi fication Class 4 Therapeutic Classificat on Class E

Autopsy Heart weight 450 Gm The heart (Fig I ) was moderately enlarged The valve rings were the seat of mild arteriosclerotic change The coronaries were slightly thickened The aorta contained a few calcified plaques Situated in the center of the posterior wall just distal to the aortic ring there as a match head ized rupture The media was split in its entirety involving the thoracic and abdominal segments to include the proximal 5 cm of the right common iliac The left renal artery was al o involved in the pro ess

## Hypertensive Cardiovascular Disease—Dissecting Aneurysm of Aorta—Survival for Five Months—Autopsy

**Case 51** A S an unemployed colored male of 60 was admitted to the Philadelphia General Hospital on 11/18/36 complaining of vertigo weakness and precordial pain



Fig 1 Dissecting aneurysm of aorta Note split in media (marked by arrow) (Autopsy No 30 3 6 Philadelphia General Hospital)

History High blood pressure for many years In 1931 he had a stroke but was able to be about again in a few months There was weakness of the left arm and leg

On 7/6/36 a sudden severe precordial pain appeared and lasted for two days It was relieved by rest in bed and medicine but returned although much less severe on several subsequent occasions Following one of the attacks the patient was admitted to the hospital




Fig 1 3 Dissecting aneurysm of the aorta A Point of rupture above aortic valve B Double aorta There were two separate channels as far as the bifurcation (Autopsy No 3 575 Philadelphia General Hospital)

Physical Examination Emaciated negro Slight dyspnea Old hemiplegia BP 210/90 Pulse 84 totally irregular Heart markedly enlarged to the left on percussion systolic murmurs were heard over the apex and aortic areas

Laboratory Data Roentgenogram hypertrophy of the left ventricle and widening of both ascending and descending portions of the aorta but no definite evidence of aneurysm

Electr ardio ram Auricul r fibrillation
Wass rmann negative

CLINICAL DIAGNOSIS A Etiologic Hypertension B Anatomic Cardiac hypertrophy Aortic dilatation Coronary sclerosis Coronary occlusion C Physiologic Auricular fibrillation Anginal syndrome D Functional Classification Class 3 Therapeutic Classification Class E

COURSE Many attacks of chest pain of the anginal type occurred from 1 /10/36 to 1?/15/36 The patient died suddenly during a severe seizure on 1 /15/36

AUTOPSY Heart weight 4 0 Gm Hypertrophy of the left ventricle with numerous fibrous scarred areas near the ap x There were atheromatous changes seen in the aorta and along the course of both coronary art ries (Fig 1 3) About 3 cm above th aort c cusp on the anterior aspect of the ascend ng branch th e as an old break in the intima leading into a separate healed channel ext nd ng to the bifurcat on (Fig 1 3) This new lumen was entirely covered by an endothelial surface The di sect on vas likewise seen to extend upward into the innominate artery form ng two separ te lum na The d sected path way opened into the right common carotid artery

# 10

# CONGENITAL HEART DISEASE

Congenital defects are rare and comprise less than 10 per cent of the cases in children s heart clinics and less than 2 per cent of all cardiac abnormalities seen in practice If these defects were listed with all their possible combinations this type of heart disease would immediately appear to be very complex Rather than wade through the intricacies of diagnosis presented by such an array it would seem easier to be satisfied with the plain diagnosis of congenital heart disease and allow the pathologists to worry about the difficulties of nomenclature and classification However during recent years the application of the newer laboratory methods and diagnostic procedures* to the problems of congenital heart disease permits a much sharper differentiation While an exact anatomic diagnosis is still a clinical impossibility in every case all patients should be carefully studied and the attempt made to record the defect that seems to be consistent with the physical signs

Aside from increasing our efficiency in cardiac diagnosis more exact knowledge of the structural defect is very useful in prognosis and in planning the patient s regime For example recently in a limited number of cases diagnosis of uncomplicated patent ductus arteriosus paved the way for the first successful ligation of this structure by Gross (page 339)

## ETIOLOGY

The chief cause of congenital heart disease is arrest of development and the earlier this occurs in embryonic life the more serious will be the resulting defect The critical time appears to be between the fifth and the eighth week just before the septa have come into apposition and the torsion of the great vessels is complete Interference in development during this period of growth will usually lead to a series of anatomic adjustments or rearrangements and multiple defects of a serious nature (morbus caeruleus) These are usually adaptations on the part of the growing embryo to permit survival in spite of grave alterations in the circulation

Interference with development at a slightly later stage before the septa *have closed (eighth week) produces localized septal defects* (cyanose tardive) while factors influencing growth after septal closure result in minor anomalies

Early writers pointed out the resemblance of many of these structural lesions to the hearts of animals and were content with the explanation of reversion to the primitive Some examples of a two-chambered heart which

* Particularly fluoroscopy

is similar to the heart of a fish appear and occasionally a three-chambered heart similar to that observed in the frog may be observed

Why this faulty development in the embryo occurs has not been satisfactorily explained but several theories have been advanced Some believe that abnormal currents in the fetal blood stream are present and prevent the septa from growing across and closing off the chambers in normal fashion Others believe that actual disease of fetal structures in the form of syphilis or tuberculosis is responsible The factor of heredity must also be given some credence since many cases live long enough to transmit the tendency Influences on the mother during pregnancy like fright operations etc are favored by the laity in the explanation of these anomalies as well as congenital defects of all types Inherent weakness of the germ plasm because of consanguinity and alcoholism must not be overlooked when we are searching for a cause in individual instances An early fetal endocarditis has been claimed to play a direct part in the formation of some of these defects but considering the evidence this seems to be a rare cause

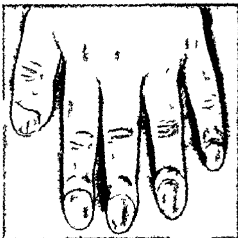
## SIGNS AND SYMPTOMS

At birth a loud murmur may be heard over the precordium If cyanosis is present a diagnosis of congenital heart disease appears quite certain However it is rarely possible at such an early date to classify the abnormality correctly If the child survives the picture becomes more clear cut and observations of the physical signs (thrills murmurs and cardiac hypertrophy) and study of the electrocardiogram and roentgenogram permit a more accurate diagnosis This does not mean that the signs present at birth should not be noted While a child s health record kept faithfully year by year is always a great asset in later life it is particularly valuable if evidence of a cardiac defect is present at birth Prolonged discussion concerning the etiology of the type of cardiac abnormality is then not so apt to arise when the murmur is heard for the first time after an attack of scarlet fever or other infectious disease of childhood As a rule murmurs heard in children under two years of age may be put down as congenital since acquired lesions prior to this age are rare

Cyanosis may or may not be present in congenital heart disease Large defects in the septum allowing considerable unaerated blood from the right side of the heart to mix with arterial blood on the left side produce cyanosis Since pressure is usually greater on the left side of the heart in small defects the direction of the flow will be from the left to the right Under special conditions however when the pressure in the pulmonary circuit becomes higher the flow may be from the right to the left for example in pneumonia after left ventricular heart failure or severe exertion This reversal of flow through the defect may cause a transient cyanosis In some congenital lesions where there is an interference with the entry of blood into the lungs (pulmonary stenosis) this additional factor contributes to

the cyanosis Cyanosis appears when the reduced hemoglobin exceeds the threshold value of 6 7 volumes per cent

Patients who have cyanosis soon develop clubbing of the fingers and toes (Fig 124) This is known as hypertrophic pulmonary osteoarthropathy (Marie 1891) While long recognized as an important sign in congenital heart disease it also occurs in subacute bacterial endocarditis and chronic suppurative conditions of the lung Infection plus obstruction to venous return seem in most cases to be the causative factors in initiating this hyperplastic process in the periosteum In congenital heart disease the clubbing of the fingers is present in direct proportion to the degree of cyanosis



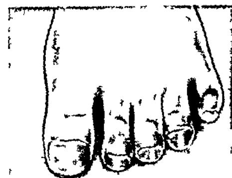


Fig 124 Clubbing of the fingers and toes

Polycythemia accompanies cyanosis and explains some of the symptoms commonly encountered in congenital heart disease When cerebral blood channels become clogged by the excess number of red blood corpuscles the patient may complain of headache and vertigo Syncope convulsions and even paralysis may follow when the degree of cyanosis and secondary polycythemia is extreme The latter symptoms are most apt to accompany a diminishing reserve and a secondary slowing of the cerebral circulation

Polycythemia results from an overactivity of the blood forming sites in their attempt to compensate for deficient oxygenation of the tissues The number of red blood cells in some cases may be increased to 12 000 000 per cubic mm The total blood volume and blood viscosity are also increased in these patients A stunted growth as well as abnormal cerebral development is not an unusual sequel in the presence of these marked circulatory defects

Symptoms of congestive cardiac failure may appear and complicate congenital heart disease at any time The incidence of pulmonary tuberculosis is also high All degrees of dyspnea may accompany congenital heart lesions, depending on the severity of the defect the amount of cyanosis

present and the activity of the patient In some defects paroxysms of dyspnea may follow exertion because of a temporary increase in the extent of the venous shunt

## CLINICAL CLASSIFICATION OF CONGENITAL CARDIAC DEFECTS

Since a variety of combinations of lesions is possible most classifications of congenital cardiac defects are lengthy and intricate There is little to be gained by attempting to remember all the types for even the more common ones are rare in the experience of any physician From the clinical standpoint it is sufficient to remember that these lesions may be conveniently grouped according to the presence or absence of cyanosis The congenital defect may offer a simple mechanical obstruction to the blood flow but no communication may exist between the pulmonary and systemic circulations Under these circumstances there is no cause for cyanosis In the next group defects in the cardiac or aortic septa may be present, but as long as the pressure remains higher in the systemic circuit blood passes from left to right and no cyanosis occurs If however the pressure is raised on the right side cyanosis appears (cyanose tardive) In the last group of cases a localized septal defect may be complicated by other anomalies which tend to raise the pressure on the venous side or one or more of the cardiovascular septa may be absent or the great trunks may be transposed A venous arterial shunt results in the development of permanent capillary changes and cyanosis Some of these cases may show a mechanical obstruction to the return of venous blood to the right heart which will cause a slowing of the capillary flow and cyanosis will result from stasis and increased de-oxygenation at the periphery

> When attempting to demonstrate that cyanosis in children may not always have a cardiac origin I depend on the story of Dr J H Means of the negro mammy who refused to alter her technic and use a thermometer to test the temperature of the white child s bath Ah can tell by de chile said she *If de* water am too hot de chile he turn red if de water am too cold de chile turn blue

Based on the above considerations Abbott[1] proposes the following classification for cardiac defects The entities marked with an asterisk I have encountered in practice and consequently I am able to summarize their outstanding features in the following pages

TABLE VIII
ABBOTT'S CLASSIFICATION OF CARDIAC DEFECTS*

I ACYANOTIC GROUP

(No abnormal communications between the two circulations)
Pericardial Defects
Ectopia cordis
* Congenital idiopathic hypertrophy
Congenital aortic and mitral stenosis
Bicuspid aortic and pulmonary valves
* Supernumerary aortic and pulmonary cusps
Double A V orifices
Coarctation of the aorta of adult type
Pulmonary dilatation
Hypoplasia of aorta
* Double and right aortic arch
Left coronary from pulmonary artery
Congenital arteriovenous aneurysm
* Dextrocardia

II CASES OF ARTERIOVENOUS SHUNT WITH POSSIBLE TERMINAL OR TRANSIENT REVERSAL OF FLOW (CYANOSE TARDIVE)

Patent ductus arteriosus
* Defects in interauricular septum
Patent foramen ovale defects in upper and lower parts of the interauricular septum
Defects in aortic septum
Congenital aneurysm sinus of Valsalva
Communications between the aorta and pulmonary artery
Defects in the interventricular septum
(Maladie of Roger)

III CYANOTIC GROUP CASES OF VENO ARTERIAL SHUNT (MORBUS COERULEUS)

A Right sided valvular lesions Fetal passages closed Stasis and increased de oxygenation in capillaries
1 Pulmonary stenosis with closed septa
2 Congenital tricuspid stenosis with closed septa
B Cases of permanent venous-arterial shunt
1 *Moderate cyanosis*
Pulmonary stenosis with patent foramen ovale
Complete absence of interventricular septum (Cor biatriatum triloculare)
Common auriculo-ventricular ostium
2 *Marked cyanosis*
Pulmonary stenosis interventricular septal defect dextroposition of the aorta and right ventricular hypertrophy (tetralogy of Fallot)
Pulmonary atresia with defect of ventricular septum and dextroposition of aorta
Cor biloculare with transposition of great trunks
3 *Extreme cyanosis*
Transposition of great trunks with closed ventricular septum ductus arteriosus and patent foramen ovale
Pulmonary atresia with closed interventricular septum ductus arteriosus and foramen ovale patent
Tricuspid atresia
Cor biloculare
Mitral atresia
Aortic atresia

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### Congenital Idiopathic Hypertrophy

Hypertrophy of the heart at birth in the absence of any intra or extra cardiac etiological factor More frequent in males Survival is generally six months to a year rarely longer

**Symptoms** Usually pallor dyspnea and cyanosis The course is down hill Death may occur suddenly

**Signs** Cardiac enlargement in all diameters (Fig 125) A systolic mur mur may be present

**Roentgenogram.** Characteristic (Fig 125)

**Electrocardiogram** Of little value unless there are associated defects



Fig 125 Roentgenogram of a one month old infant Note marked cardiac hypertrophy Autopsy showed von Gierke's glycogen storage disease

**Present day Views** The discovery of other causes for congenital hyper trophy is decreasing the number of cases labelled 'idiopathic In 1929 von Gierke's glycogen storage disease (cardiomegaly glycogenica) was described Deposition of large amounts of glycogen in the heart as well as in other organs (liver kidneys brain) occurs Anterior pituitary dysfunc tion and consequent defect in the glycogen splitting ferment has been ad vanced by some investigators as a cause for this rare disease which repre sents a persistence of the conditions that characterize fetal metabolism Glycogen can be readily demonstrated in the organs by the use of Best s carmine stain

**Treatment** At present there is no treatment known to control this per version of metabolism that results in structural changes in so many organs

BICUSPID AORTIC AND PULMONIC VALVES SUPERNUMERARY PULMONIC CUSPS



FIG 126 A Bicuspid aortic valve Secondary bacterial endocarditis ulceration and perforation This patient a white male of 46 developed aortic regurgitation while under observation in the hospital This was followed immediately by congestive cardiac failure Death occurred five days later The clinical diagnosis was syphilitic cardiovascular disease although the Wassermann was negative (Autopsy No 4773 Philadelphia General Hospital)



FIG 126 B Bicuspid aortic valve In this case the aortic valve was the seat of extensive deposits of calcium A terminal subacute bacterial endocarditis is seen (Autopsy No 33661 Philadelphia General Hospital)



FIG 1 6 C Supernumerary pulmonary cusps

1 Bicuspid Aortic Valve This defect per se does not produce any signs or symptoms However it is not without significance clinically since these valves very frequently become the seat of sclerotic change subacute bacterial endocarditis or both (Figs 126A and 126B) In some of these cases the aorta immediately above the valvular defect may show *dilatation*, dissection, and secondary rupture

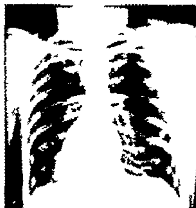
2 Supernumerary cusps are more frequently encountered at the pulmonary orifice where they are not often the seat of invasion and consequently are of little clinical significance A quadricuspid aortic valve is of more importance owing to the likelihood of the development of subacute bacterial endocarditis

### Congenital Dextrocardia

1 True dextrocardia (situs inversus) The heart is on the right side and the other viscera are likewise transposed

2 Dextrocardia without transposition of the other viscera is rare Its association with other anomalies generally determines the prognosis in each instance

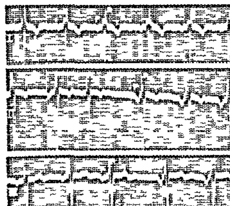
A



Clinical Diagnosis

Possible if palpation and percussion routinely practiced to the right as well as to the left of the sternum

B



All waves in lead 1 are reversed in direction Note that lead 3 is equivalent to lead 2 and 2 to 3

Fig 127 A Congenital dextrocardia B Electrocardiogram of patient who had congenital dextrocardia and acquired mitral stenosis (see Fig 77)

Dextrocardia is unimportant if no other cardiac defects co-exist It does not shorten life There are no symptoms

## Interventricular Septal Defect (Roger's Disease)

**Usual Site** High up in the fibrous part of the septum (See Fig 132)

**Direction of Blood Flow** From left to right Reversal of flow may take place during terminal stages with cyanosis

**Heart** Enlargement may be present or absent Murmur is loud, harsh *and systolic in time Point of maximum intensity is the third or fourth* intercostal space close to the sternum A thrill is palpable over this area

**Electrocardiogram** In rare cases the defect involves the conduction system and causes heart block (page 345)

**Prognosis** Depends on associated defects and heart size The danger is subacute bacterial endocarditis (Case 87) Interventricular septal defect is one component of Fallot's tetralogy (page 347)

Note If the coronary artery supplying the interventricular septum becomes occluded in later life and the infarct softens and ruptures an acquired interventricular septal defect may appear It is usually small and unimportant but may produce physical signs similar to the congenital type

## Coarctation of Aorta

**Types** 1 Infantile Narrowing of the isthmus of the aorta between the left subclavian and the ductus arteriosus (Rare)

2 Adult Narrowing of the aorta at the site of the ductus arteriosus (Common type)

**Symptoms** Variable often none There may be intermittent claudication in the absence of demonstrable arterial disease

**Cardiac Signs** Hypertrophy Followed at times by signs of failure

**Electrocardiogram** Not characteristic

**Diagnosis** Not difficult if the possibility is kept in mind and the characteristic features are sought

### Vascular Signs

Hypertension in upper extremities

Decrease in blood pressure in lower extremities Collateral circulation occurs through anastomoses of internal mammary and epigastric arteries and through dilated intercostal vessels (Fig 128C)

Tortuous or pulsating arteries may be seen or felt under the skin in posterior wall of the thorax around the scapula or in the anterior abdominal wall

Thrills and murmurs may appear along the course of these vessels

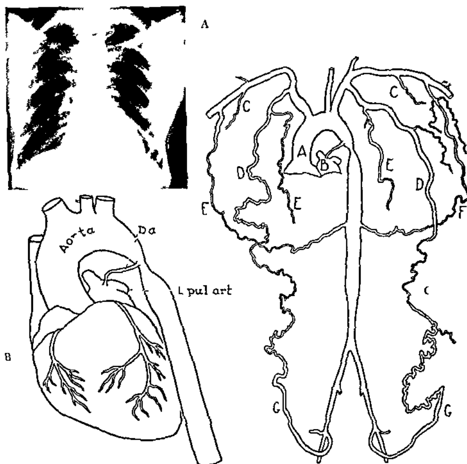



FIG 1 8 A Roentgenogram n coarctation of the aorta Characteristic scalloping of the inferior margins of the ribs se n Th s is caused by eros on of bone by dilated *inter o tal a teries* (*Courtesy of Dr Paul A B shop*) *B Draw ng of coarctation of th* ao ta of the adult type Note marked narrowing of the aorta just below point of in s rtion of d ctus arte iosus C Collateral circulation in a case of coarctation of the aorta (A Aorta B Pulm onary artery C Subscapular artery D Internal mamma y artery E Thyro d artery F Int rco tal artery G Ep gastr c artery)

### Patent Ductus Arteriosus (Commonest congenital defect)

**Etiology** The ductus may remain open to compensate for the other defect (coarctation) consequently it is less often found uncomplicated

**Direction of Flow** Pressure in the aorta is higher therefore the flow is from the aorta to the pulmonary artery (arteriovenous shunt)

**Symptoms** Usually none

A



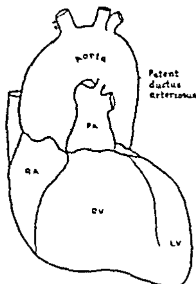
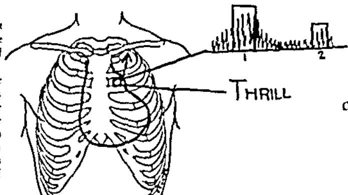



Fig 1 9 A Roentgenogram in patent ductus arteriosus Note the great dilatation of the conus pulmonale This is more extreme than that noted in mitral stenosis Some enlargement of the heart to the left is also seen B Diagram showing patent ductus arteriosus C Chart of physical findings




C

### Signs

Continuous murmur and thrill at the second left interspace near the sternum

The heart shadow in marked cases shows enlargement of the pulmonary artery, and hypertrophy of all chambers of the heart may be present

Increased pulse pressure and the peripheral signs may be present as in aortic regurgitation In the case of patent ductus arteriosus the regurgitant stream goes into the pulmonary artery

**Prognosis** Depends upon the size of the communication Surgical ligation is possible in selected (uncomplicated) cases (page 339)

In fetal life the blood is short-circuited around the lungs from the pulmonary artery to the aorta through the ductus arteriosus (Fig 129B) When the lungs expand after birth the ductus normally closes and becomes atrophic If it remains open the blood flow through this structure is reversed

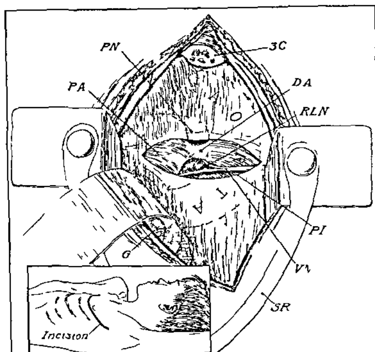



FIG 130 Sketch of operative exposure of the ductus which was 11 mm in diameter Insert shows position of the patient with the left arm drawn up along the head and with incision coursing just beneath the breast Thorax entered through the third interspace Third cartilage cut to allow upward retraction of ribs The left lung is held down inferiorly with a gauze pack and malleable retractor Positions of aorta and pulmonary artery indicated by dotted lines When the pleural covering of the mediastinum was incised a direct view of the aortic arch pulmonary artery and ductus was obtained (3C) Cut end of third costal cartilage DA Ductus arteriosus G Gauze pack over collapsed lung PA Pulmonary artery PI Pleural incision PN Phrenic nerve RLN Recurrent laryngeal nerve SR Self retaining retractor VN Vagus nerve

since the pressure in the aorta is greater than in the pulmonary artery If the passageway is large the effect on the circulation is the same as that of any other arteriovenous aneurysm or shunt About two-thirds of the patients who have a patent ductus arteriosus show an associated anomaly but in one third of the cases the patent ductus exists as the only defect Recently the latter group has assumed considerable importance since Gross has demonstrated that this arteriovenous communication can be successfully ligated (Fig 130)

While in some instances uncomplicated patent ductus arteriosus may be compatible with a normal life in Abbott's series of 92 patients showing this defect 2 died of subacute bacterial endocarditis 24 of cardiac decompensation 16 of sudden heart failure and two of sudden rupture of the ductus The average age at death was 24 years Consequently the reason for employing surgical measures in these selected instances is to improve a most uncertain future The patient who has an uncomplicated patent ductus arteriosus faces the danger of developing subacute bacterial endocarditis or endarteritis at any time If this complication is avoided the possibility remains that the shunt may increase in size and cause cardiac hypertrophy and subsequent failure In a few cases the patent ductus may dilate and become thin walled in which event the danger of rupture is not negligible These ever present threats are eliminated by ligation

Before recommending operation the presence of associated defects such as aortic stenosis or coarctation stenosis or atresia of the pulmonary artery or the complication of bacterial endocarditis should be ruled out Pulmonary stenosis may offer some difficulty in the differential diagnosis although the presence of a loud pulmonic second sound in cases of patent ductus and its absence in disease of the valve is an important point in drawing the distinction In pulmonary stenosis a right axis deviation appears in the electrocardiogram while cardiac hypertrophy and cyanosis are more apt to be present Associated anomalies like septal defect or a mitral stenosis if slight are not contraindications to operation for as Cross points out some improvement may follow if one defect is corrected Vegetations of a subacute bacterial endocarditis present near the opening of the ductus arteriosus may be dislodged at the time of the operation consequently their presence should be regarded as a complication

In some cases where patent ductus arteriosus is the single lesion spontaneous closure in later life may take place If the findings are at all suggestive of this occurrence operation should not be considered In the absence of cardiac enlargement in patients who have a normal diastolic pressure and only a slight fulness in the region of the pulmonary artery on fluoroscopy operation likewise has little to offer When the heart is increasing in size and the physical findings are becoming more pronounced as the child grows older operation is indicated

## SUMMARY OF CRITERIA FOR OPERATION (CROSS)

1 Presence of machinery murmur in pulmonary area accompanied by increase of P2 most intense in the same area

2 Congestion of the lung fields in the roentgenogram

3 Prominent pulmonary artery in roentgenogram

4 Roentgenologic evidence of cardiac enlargement particularly in the region of the left ventricle

5 Systolic blood pressure normal with a lowered diastolic level

The operation recommended and successfully carried out by Cross

exposes the ductus from the left side The pleural cavity is entered, the lung collapsed, and the structures in thi manner adequately exposed (Fig 130) Gross reports little postoperative reaction no important postoperative complications and no mortality in his first four cases In each patient following operation the thrill disappeared and the diastolic pres ure ro e to a normal level In two instances the transverse cardiac diameter decreased and one undernourished child gained nine pounds following ligation After the procedure each child returned to school with a much improved circulation

## Interauricular Septal Defects

**Entire absence of auricular septum** may occur but is very rare (cor triloculare biventriculare) (page 343)

**Persistent ostium primum** follows arrested development of septum primum and is seen in the lowest part of the interauricular septum (Fig 131)

**Patent foramen ovale** is more frequently encountered A valve like opening is seen in 25 per cent of autopsies but is unimportant When the foramen ovale remains widely open because of a defect in the ostium secundum it is significant This defect often accompanies persistent ostium primum

If not associated with other defects there may be *no signs or symptoms* Subacute bacterial endocarditis *is rare in this region* but paradoxical embolism may occur Thrombi from veins pas ing through the interauricular septal defect tend to lodge in the systemic circulation Emboli may also go from the left auricle to the lung through this septal opening

**Case 52** (Fig 131) A poorly nourished white female baby six months of age was admitted to the Philadelphia General Hospital for bronchopneumonia Examination of the heart was entirely negative Death occurred on the eleventh hospital day following the complication of acute otitis media Cyanosis was present shortly before death

Autopsy showed interauricular septal defect as the only congenital anomaly Death was caused by bronchopneumonia acute otitis and sepsis



Fig 131 Interauricular septal defect (Autopsy No 4 099 Philadelphia General Hospital)

### Patent Foramen Ovale Defects in Interventricular Septum Autopsy

**Case 53** An emaciated colored female child of four was admitted to the Philadelphia General Hospital complaining of shortness of breath and cough of four months duration

Physical Examination showed precordial bulging precordial thrill over the third left interspace and a loud rough systolic murmur in the same region The liver was two fingers breadth below the costal margin Wassermann negative

Autopsy Cardiac hypertrophy Patent foramen ovale Three separate openings between the left and right ventricles were discovered in the upper portion of the septum (Fig 152) No other defects



Fig 152 Interventricular septal defects (Autopsy No 364 Philadelphia General Hospital)

## ILLUSTRATIVE CASES

### Complete Absence of Interauricular Septum and of the Membranous Portion of the Interventricular Septum—Congenital Heart Block—Autopsy 04 16

**Case 54** An infant boy age six hours th sixth child of a woman age 8 was admitted to the Woman s College Hospital on May 6 193 The father and mother and the other ch ldren were free of congen tal defects The mother s prenatal period was entirely uneventful and the del very was norm l The Wassermann reaction of the mother s blood was negative

On admission the infant was well developed and well nourished and as apparently a f ll term baby No defects were noted The weight was eight pounds (3 630 Gm) There was inten e cyanosis of the body generally and of the lip ears and nails especially Examination of the lungs show d mpaired resonance at the left apex poster orly The breath sound were harsh over both lung fields and there were many crep tant rales throughout Substernal inspiratory retraction was present The left border of the heart was 7 cm from the mid ternal line in the fourth interspace The right border was 5 cm from the m d te nal line in the fourth nterspace The fir t sound was obscured by a blo ving systolic murmur and the second sound was eak The murmur was audible over the nt re chest but th center of intensity was in the second interspace at the left of the sternum The rate of the heart beat was 40 per minute There ere no thrills The liver and spleen were not palpable and the rest of the examinat on was negative

The child was taken to the heart stat on of the hosp tal where electrocardiograms w re made at intervals for the next fe hours All tracings showed complete heart block with the ventr cular rate of 50 the auricular rate of 100 and low voltage (Fig 133B) Oxygen was administered ith sl ght improvement in the cyano s The electrocardiogram was not alte ed

The ch ld wa taken back to the ward and kept in an oxygen tent A roentgenogram of the chest (Fig 133A) showed the heart shado to be very large in all diamete The child d ed 18 hours after it b rth

Diagnosis A Et olog c Cong nital defect B Anatomic Card ac hypertrophy Interv ntricular septal d fect C Phys ologic Complete heart blo k D Funct onal Class fication Class 4

Autopsy The main defect of the heart was th al no t complete ab nce of the nter a r cular septum and the membranou port on of the terventri ul r septum The coronary veins em pt ed separat ly into the m ddle of th po ter o wall of the common auricle The venae cavae had a common openi g The m t al and tr cu p d valves were completely fo med and were attache l m d ally to the upper edge of the interventricular septum The aorta and pulmonary arte y had approximately normal relat onsh p

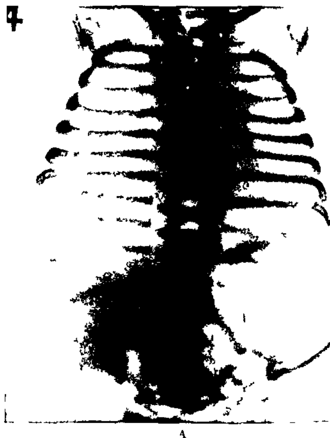
Microscopically t was obse ved by means of serial sect ons that there was practically complete abse ce of the conduct on bundle between the common auricle and the ventricles The d fect had completely severed the aur culove itr cular nod from the auriculo ventricular bundle Th bundle of H s and the left bundle branch were well developed but a definite r ght bundle branch ould not be found although there was a suggestion of one

**Discussion** In this case we have an example of a three chambered heart with one auricle and two ventricles (cor triloculare biventriculosum) Other cases of heart block of congenital origin associated with this anomaly have not been reported

A complete block of the contraction impulse from the auricle occurred in the upper third of the interventricular septum at the site of the defect

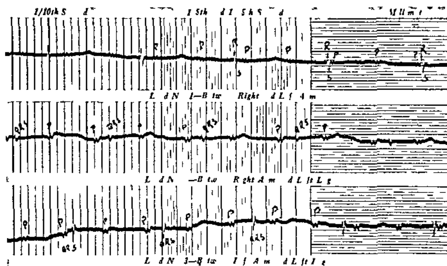
This anatomic separation was shown to be of developmental and not of inflammatory origin by serial sections The bundle of His was well formed but was disconnected from the auriculoventricular node in the region of the defect

The clinical diagnosis of congenital heart block is not difficult When the presence of auriculoventricular dissociation is proved by an electrocardiogram taken shortly after birth a defect in the upper third of the inter ventricular septum is at once suggested In this patient the cyanosis cardiac



A

Fig 133 A Roentgenogram taken four hours before death Note enlargement of the heart in all diameters B Electrocardiogram Complete heart block is present The auricular rate is 100 and the ventricular rate is 50 C The interior of the heart bisected in sagittal plane A the posterior half; B the anterior half VS interventricular septum RV right ventricle; TV tricuspid valve; CV openings of coronary veins in auricle; RC right coronary artery RA portion of the common auricle corresponding to normal right auricle; VC common orifice of vena cavae; AS spur in roof of common auricle dividing it incompletely into right and left halves; LA portion of the common auricle corresponding to normal left auricle; *MV mitral valve; LV* left ventricle PC pulmonary conus, AV aortic orifice under anterior leaflet of the mitral valve



B

AS
RA
AS
LA
VC
PC
TV
RA
AV
RC
VS
CV
TV
RV
MV
LV
VS
LV

C

enlargement and the systolic murmur were physical signs in keeping with this impression The clinical recognition of the other abnormalities associated with the interventricular septal defect in this case was, of course, impossible

The diagnosis of congenital heart block in older children in addition to the typical electrocardiogram rests upon the history of bradycardia at a very early age and the absence of an infection that might cause heart block after birth such as rheumatic fever chorea diphtheria or congenital syphilis The occurrence of syncopal attacks at an early age is fairly good evidence of the existence of heart block prior to the attacks

### Pulmonary Stenosis

Complete atresia may be present (page 348) or the pulmonary valve may be markedly stenosed the pulmonary artery small and the right ventricle large Associated septal defects are very common because of obstruction of the blood flow from the right ventricle and are in some measure compensatory Pulmonary stenosis is a component of Fallot's tetralogy (page 347) In complete atresia the blood may reach the lungs through a patent ductus arteriosus If this is absent dilatation of the bronchial arteries usually occurs Uncomplicated pulmonary stenosis is rare

**Signs** Cyanosis stunted growth clubbed fingers polycythemia thrill and harsh systolic murmur in the second or second and third intercostal spaces just to the left of the sternum The pulmonic second sound is diminished or absent

**Electrocardiogram** Marked right axis deviation is encountered in addition to the large P waves that are associated with right auricular enlargement (Fig 135)

### Tetralogy of Fallot

(Most common cause of congenital cyanosis in patients surviving to adult life)

The combination of defects that makes up the tetralogy consists of

1 Ventricular septal defect
2 Pulmonary stenosis
3 Dextroposition of the aorta
4 Hypertrophy of the right ventricle

If pulmonary stenosis develops before the septum closes blood is shunted from the right to the left side of the heart and then to the aorta which is dextroposed This is followed by hypertrophy of the right ventricle Cyanosis is always present

Signs A systolic murmur is present over the precordium and is most intense over the pulmonary area There is a systolic thrill in the pulmonary area

Electrocardiogram Right axis deviation

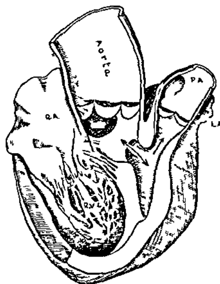



Fig 134 Schematic drawing illustrating Tetralogy of Fallot

Roentgenogram Diminished prominence of the pulmonary conus with elevation of the apex by enlargement of the right ventricle may give coeur en sabot appearance (Figs 29 and 136)

PULMONARY STENOSIS ASSOCIATED WITH PATENT FORAMEN OVALE—AUTOPSY

**Case 55** A white American male 22 years of age was admitted to the Tuberculosis Division of the Philadelphia General Hospital complaining of cough hemoptysis and dyspnea Extensive tuberculous invasion of both lung apices was found and the sputum was positive for tubercle bacilli There was a systolic thrill and murmur over the pulmonary area The fingers were clubbed Cyanosis was present

AUTOPSY Heart weight 420 Gm The pulmonic valve had two cusps and showed marked stenosis Foramen ovale patulous No other defects

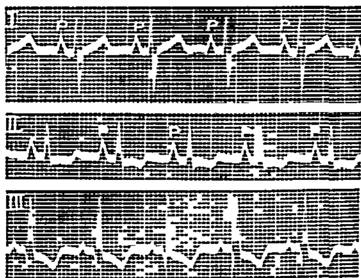



FIG 135 The electrocardiogram in congenital pulmonary stenosis Note high pointed P waves in the first two leads Right axis deviation is present

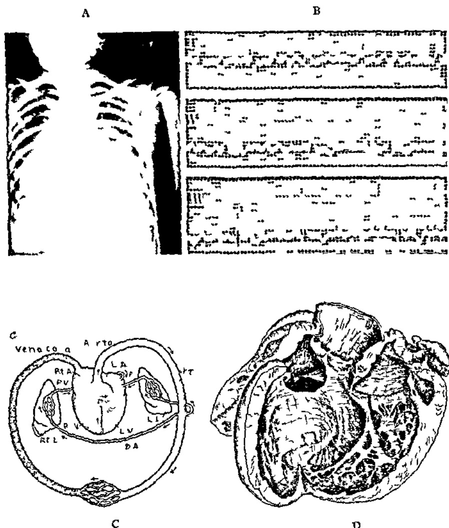



FIG 136 A Roentgenogram of chest Note "coeur en sabot" appearance of cardiac silhouette There is considerable enlargement of all chambers B The electrocardiogram Auricular fibrillation is present Right axis deviation C Diagram illustrating circulation in Case 56 The aorta is dextroposed The bronchial arteries (B A) supply the lungs They arise from the descending aorta at the level of the trachea (T) There is complete pulmonary atresia Interventricular septal defect is also present D Drawing of specimen Note hypertrophy of the right ventricle complete pulmonary atresia dextroposition of the aorta and interventricular septal defect

## ILLUSTRATIVE CASE

### Complete Pulmonary Atresia with Defect of Ventricular Septum Dextroposition of the Aorta and Hypertrophy of the Bronchial Arteries—Autopsy [10]

**Case 56** A cyanotic male child of five was admitted to Memorial Hospital complaining of shortness of breath and vomiting. He was well until four months before admission when he had a sudden convulsive seizure following exercise. Dyspnea fatigue and cyanosis appeared for the first time. A second convulsive seizure the day before admission was followed by edema dyspnea and vomiting.

Physical Examination BP 90/60 Pulse 1[illegible]0 totally irregular. Cyanosis. Dyspnea. Edema of the extremities to the knees. Marked bulging of the left side of the chest. Apex beat in the anterior axillary line in the sixth interspace. There was a thrill palpable over the third intercostal space to the left of the sternum. A systolic murmur was heard over the whole precordium loudest in the region of the thrill. Systolic and diastolic murmurs were present over the cardiac apex. The liver edge extended to the umbilicus. No ascites. Dulness of the right chest posteriorly to the scapular angle. Fingers and toes showed marked clubbing (See Fig 1[illegible]4).

Laboratory Data Blood count hemoglobin 1[illegible]0 per cent (Sahli); R B C 6 410 000; W B C 6 700; Differential normal. Wassermann and Mantoux tests negative. The urine showed a light cloud of albumin and 3 R B C per H P F.

Electrocardiogram (Fig 136B) auricular fibrillation and right axis deviation.

Roentgenogram (Fig 136A) heart enlarged in all diameters. Note "coeur en sabot" outline. A concavity replaces the curve in the left border usually formed by the pulmonary artery.

Clinical Diagnosis A Etiologic Congenital Tetralogy of Fallot (?) B Anatomic Cardiac enlargement Interventricular septal defect pulmonary stenosis right sided aorta C Physiologic Congestive cardiac failure Auricular fibrillation. D Functional Classification Class 4 Therapeutic Classification Class F

**Discussion** Bed rest and digitalization resulted in slight improvement. Three days after admission there was a sudden attack of dyspnea progressing to orthopnea during which the cyanosis became extreme and marked distention of the neck veins appeared. A venesection (300 cc) was performed and the patient was placed in an oxygen tent. Theoretically oxygen administration should not be expected to relieve the cyanosis of congenital heart disease. However some improvement was noted in this instance. The digitalis was cut to a maintenance level of 2 grains daily on the eighth hospital day. The liver appeared to be much smaller in size. During the third week in the hospital death occurred suddenly following a third convulsive seizure.

This patient shows that little decrease in the exercise tolerance is possible in some instances in the presence of marked derangement in anatomic structure. This lad lived on the third floor of a city apartment house where there was no elevator. It is remarkable that he was able to climb these steps many times daily without the appearance of cardiac symptoms. Unfortunately, he was also allowed to engage in active play with other children and this contributed to the rapid breakdown of his reserve. The slowing of the cerebral circulation in the early stage of failure in the presence of the polycythemia precipitated the convulsive seizure. Following this the decline

was rapid The persistent vomiting that preceded his admission to the hospital probably was caused by stasis of the circulation and the clogging of the blood channels along the gastro-intestinal tract

The congestive failure was treated in the same manner as failure caused by any other type of heart disease Death occurred following a convulsion and was attributed to cerebral thrombosis

Four other examples of complete pulmonary atresia with closed ductus arteriosus and a pulmonary circulation carried on through dilated bronchial arteries have been previously described in the literature The ages of death of these patients were 33 30 20 and 6 years all surviving longer than this patient Two of the patients in the series died following intercurrent infections, while thrombosis in the bronchial arteries was the cause of death in the other two The patient showing the smallest bronchial arteries died in childhood so it may be said that the larger the bronchial arteries in the presence of complete pulmonary atresia the better the chance of survival

The occurrence of auricular fibrillation in this patient is worthy of note for the arrhythmia is very rare under the age of 15 It is likewise seldom seen associated with congenital heart disease However while advanced cardiac disease of any type may be present without the occurrence of auricular fibrillation when congestive failure occurs with its auricular strain fibrillation may appear at any age

There is some excuse for mistaking complete pulmonary atresia for the tetralogy In the first place if the ductus arteriosus is closed the coeur en sabot appearance of the roentgenogram suggests the latter diagnosis when other manifestations of congenital heart disease are present When the interventricular septal defect is small and the murmur loud and well transmitted to the base of the heart differential diagnosis becomes most difficult if not impossible However in the absence of a murmur and thrill over the pulmonary area in patients showing this typical roentgen ray picture in addition to dextroposition of the aorta polycythemia and clubbing the diagnosis of complete pulmonary atresia is to be thought of If the patient is an adult greatly enlarged bronchial arteries can be pre dicted

## TREATMENT

When patients who have congenital cardiac disease survive the period of childhood the greatest threat to life is the development of subacute bac terial endocarditis at the site of the malformation In many of the cases the defects are otherwise compatible with a long existence and in this respect resemble healed rheumatic lesions Subacute bacterial endocarditis is most apt to be superimposed on interventricular septal or aortic defects patent ductus arteriosus or bicuspid aortic valves The blood flow through the abnormal shunts in time produces fibrosis and thickening about their margins and on the walls of the right ventricle and pulmonary artery

*These are ideal locations for the growth of micro-organisms* Auricular septal defects escape this danger Following tonsillectomy dental extractions or any other operative procedure when a temporary blood stream invasion is apt to occur sulfanilamide or one of its derivatives should be administered (page 196)

The treatment of congenital heart disease lies chiefly in the prevention of complications These children should be guarded against infections of all types in much the same manner as the rheumatic group Upper respiratory infections or focal infections in teeth tonsils or sinuses and all minor ailments should be carefully managed and always regarded more seriously in children who have congenital heart disease than in normal children Pulmonary tuberculosis is a danger particularly in patients who have defects of the pulmonary artery

Children who have serious defects and permanent cyanosis should never be allowed to attend public schools where the temptation is present to compete with normal children Special schools that provide individual attention are needed The acyanotic group may attend school but should not be allowed to engage in competitive athletic activities Exercises that do not produce cyanosis or dyspnea however may be allowed

Careful medical supervision is needed in order that the problems of *management may be intelligently met as they arise Children who have* congenital lesions should be frequently examined at the time of puberty, when rapid growth adds another burden to the circulation

Proper guidance during early years especially in the selection of a suitable occupation that will not place too great a strain on the circulation in later life or expose the patient needlessly to changing weather conditions is very important

In the cyanotic group the treatment can only be palliative since the oxygen unsaturation eventually creates a train of complications all of which tend to influence the course unfavorably Sudden death is not infrequent in many cases of this group It may also follow spontaneous rupture of the aorta or cerebral hemorrhage in patients who have coarctation When we consider the group of patients suffering from congenital heart disease as a whole the most common cause of death is found to be congestive failure (Case 56) Its management is the same as outlined for other types of heart disease with the exception of the fact that when congestive manifestations appear in congenital heart disease the outlook is exceedingly poor

## PROGNOSIS

The prognosis in congenital defects in the absence of cyanosis and clubbing is good as far as the lesion itself is concerned The complications however, are always a threat and therefore prognosis should be guarded If the only abnormality is patent ductus arteriosus operation offers a possibility of cure unless this lesion compensates for some other defect

# 11

# THE HEART IN THYROID DISEASE

The cardiac mechanism may be influenced by disorders having their origin elsewhere in the body Chief among these are disturbances of the thyroid gland which may be accompanied by either excessive secretion (hyperthyroidism) or a deficient secretion (hypothyroidism) In either of these conditions the cardiac symptoms may so overshadow the rest of the clinical picture that a diagnosis of some form of primary heart disease may be made Consequently successful management will depend on recognition of the correct etiologic background

## HYPERTHYROIDISM

Hyperthyroidism or thyrotoxicosis may appear in patients with the nodular type of goiter (toxic adenoma) or it may develop as a part of the classical picture of exophthalmic goiter In either instance the same secondary disturbances take place in the circulation In nonendemic areas the incidence of the thyrotoxic state depends upon the ability of the physician to recognize the early symptoms of the disease White[393] found hyperthyroidism to be the main factor in producing cardiac symptoms in 5 per cent of his patients

**The mechanism** by which thyroid secretion in excessive or toxic amounts affects the myocardium has been long debated Some authorities claim that it is merely an exhaustion state the end result of overaction of the organ induced by the elevated metabolic rate Others claim that a specific myocardial lesion is produced but much doubt remains concerning the existence of such a structural change Most of the abnormalities that have been described are merely incidental and do not appear to be specifically related to the thyroid hyperfunction

### Signs

There is a wide variation in the clinical picture produced in different patients by the same degree of thyroid overactivity The main symptoms palpitation and tachycardia may be present continuously when secondary to a sinus tachycardia or paroxysmal when arising from episodes of auricular fibrillation or flutter Palpitation may be mild at first appearing only after exertion Later the rapid heart rate that produces palpitation may be present at all times

In older patients who have already some degree of coronary sclerosis the added burden of thyrotoxicosis may be just enough to accentuate this underlying defect, and angina may appear

Some patients will show a quick progression of the disease with the early appearance of edema and other congestive manifestations In this group the thyroid background may be entirely overlooked in the presence of other coincidental factors such as hypertension or coronary disease It is therefore *most important to be continually on the lookout for this type of case,* for if the correct etiology is discovered proper treatment may restore the patient to normal activity for an indefinite period Some observers contend that these advanced symptoms of congestive failure are not produced by the action of the excess of toxic thyroid secretion on a normal heart but appear only in the presence of a previous cardiac lesion of rheumatic sclerotic or hypertensive type The hyperthyroidism in these cases acts merely as the precipitating factor These primary conditions, of course do not disappear following successful treatment of the thyroid disorder

## Pathology

When the pathologist views the thyroid heart at autopsy he can point to no specific lesions that characterize the condition Slight enlargement of the heart is the rule and there is usually an increase in the size of the individual muscle fibers but the various chemical changes responsible for the abnormal cardiac action elude detection No necrotic areas or inflammatory changes are encountered in the endocardium myocardium or pericardium

If we view the heart in this condition as only one organ of the body *that is influenced by a generalized disturbance the symptoms* will be better understood The increased metabolism speeds all bodily processes which naturally places a demand on the heart for more blood the amount being governed by the degree of elevation of the metabolism A normal heart can usually meet these demands indefinitely while a diseased organ will show hypertrophy and ultimately failure will appear Some observers[36] view the heart in hyperthyroidism as a circulatory problem quite similar to the arteriovenous aneurysm since all vascular channels in the thyroid are widely dilated

## Incidence

Hyperthyroidism may appear at any age The average reported by Hurxthal[165] is 37 while in a series reported by White and Jones[393] 56 per cent were found to be between the ages of 30 and 50 In all the groups studied women predominate although usually men show the more severe cardiac reactions While race has little influence on the incidence of thyrotoxicosis, the incidence reported among negroes is low

## Diagnosis

Examination of the thyrocardiac patient reveals an increase in the rate and force of the heart action The apex beat is usually readily visible and the palpating hand will detect an increased force of the cardiac impulse

An axillary impulse may be seen at times in the presence of an overactive heart and care should be taken that this is not interpreted as evidence of hypertrophy Increased pulsation of the vessels of the neck may also appear The entire picture of overaction is reflected in the cardiac silhouette at the time of the fluoroscopic examination and this observation serves as valuable suggestive evidence Systolic murmurs are not uncommon in thyrotoxicosis particularly over the region of the pulmonary artery while increase in the size of this vessel and in the entire pulmonary circulation may appear in advanced stages of the disease (see Fig 139)

Examination of the neck in most cases reveals some enlargement of the thyroid gland and the well known eye signs (exophthalmos inability to converge widening of palpebral fissures and lid lag) may be in evidence All of these may be absent and the patient may show only a peculiar staring expression which is just as valuable an observation The skin of the thyrocardiac patient is warm moist and flushed and quite characteristically elastic even though he may have lost 30 to 40 pounds in body weight The patient s attitude is alert and the motions are quick nervous and at times purposeless The pulse is rapid averaging about 110 The rhythm of the pulse at first is regular (sinus tachycardia) later becoming irregular owing to the presence of premature beats or paroxysms of auricular fibrillation or flutter These paroxysms may recur with increasing frequency until the arrhythmia usually auricular fibrillation becomes established The patients who show congestive failure quite often have auricular fibrillation as a complication

**Blood Pressure Change** The most constant change in the blood pressure is an increased pulse pressure caused by a fall in the diastolic level and a less constant elevation of the systolic reading Evidence of this increased pulse pressure is seen in the dancing of the arteries on physical examination and in the increased range of cardiac contractions on fluoroscopy The increased pulse pressure may give a Corrigan pulse and other peripheral signs

**The electrocardiogram** in thyrotoxicosis reveals the nature of any arrhythmia that may be present but it does not have a pattern that is characteristic of the condition High T waves are often observed but are not invariably present in fact T may at times be inverted An uncomplicated sinus tachycardia is the usual finding on electrocardiographic examination in hyperthyroidism

Determination of the **basal metabolic rate** is a reliable diagnostic procedure if carefully carried out by an intelligent technician More than one estimation should be made Usually the basal metabolic rate in thyrotoxicosis will be from 30 to 75 per cent above the normal Other laboratory tests may be of value in the diagnosis of thyrotoxicosis when doubt exists The blood cholesterol values tend to be definitely diminished in hyperthyroidism there is also a decrease in creatine tolerance [66] an increase in the rate of the circulation and the blood volume

In younger patients the diagnosis of thyrotoxicosis is not difficult when

the expression is staring and there is exophthalmos, tremor, sweating, and enlargement of the thyroid gland In elderly patients the condition is more apt to be overlooked since the gland enlargement may be absent or hidden beneath the sternum or the sternomastoid muscle the eye signs few and the flushing less noticeable A careful search however, may show a fine tremor

**The loss of weight** is usually marked even though the patient has a splendid appetite and consumes hearty meals The recognition of this fact serves to differentiate the condition from other wasting diseases The elderly patient with thyrotoxicosis who comes to the physician complaining of dyspnea chest pain weakness palpitation or edema is quite apt to have an associated arteriosclerosis It is important therefore to keep the possibility of thyrotoxicosis constantly in mind and to make a careful search for additional clues in older patients

**The signs of mitral stenosis** may be imitated by the overactive heart of thyrotoxicosis The first sound at the apex will be accentuated in both conditions but the thrill and the murmur in mitral disease are diastolic This usually serves to make the distinction However mitral stenosis may be present occasionally with superimposed thyroid disease (see Case 16) in which event other signs must be relied upon Digitalis will not so readily slow the rapid fibrillation that accompanies thyrotoxicosis and this observation often leads to the detection of the thyroid background The reduction in the pulse rate in thyrotoxicosis that follows the administration of iodine is another therapeutic test of value

## Course

The course of the thyrotoxic process in any patient depends on a number of factors age sex social position duration of the symptoms and the presence or absence of another form of heart disease The last circumstance may predispose to the early appearance of heart failure while hyperthyroidism in younger patients with normal hearts may be well tolerated for many years

## Treatment

Many forms of treatment have been recommended for thyrotoxicosis When cardiac manifestations are prominent and progressive however there is only one surgery Subtotal thyroidectomy brings quicker and more certain restoration of health and for this reason is the best procedure particularly in patients who have to earn their own living

Much has been claimed for the cures achieved by continuous medical management but these are uncertain and often hard to evaluate properly, since the course of the disease in many patients shows a natural tendency to remissions Many patients cannot afford to take the long rest periods that this course of treatment entails Surgical relief is eventually sought in most cases so in the long run when cardiac symptoms are present nothing is gained by delay Where the diagnosis is in doubt or where the

condition shows a tendency *to run a very mild course* sedatives rest and psychotherapy may prove beneficial

**Pre operative Treatment** Medical management however is most essential in the preparation of the patient for surgery Rest in bed and the administration of iodine in some form over a period of two weeks prior to operation constitute a regime of recognized value The form of the iodide is not a matter of importance Potassium iodide (KI) 0.3 to 0.6 Gm (5 to 10 grains) *or* Lugol s solution in 0.3 cc to 1.8 cc (5 to 30 minim) doses three times daily may be given In about 10 days marked improvement in the patient s condition will take place and this is reflected in the slowing of the pulse the reduction in the basal metabolic rate and improvement in all the symptoms of thyrotoxicosis Operation during this temporary period of induced calm can be performed with much less risk

Sedatives should be used during this preparatory regime to secure proper rest and thiamin chloride (vitamin $B_1$) should be given The best time for operation is determined by observing the pulse the basal metabolic rate and the weight in each individual Usually a period of 10 days is sufficient in uncomplicated cases

Digitalis should be given pre-operatively in every case of congestive failure regardless of the presence or absence of auricular fibrillation The amount of digitalis tolerated by a patient who has a greatly increased metabolic rate is of course much higher than can be administered safely to another patient of the same weight who has a normal basal metabolic rate

*Auricular fibrillation is present in about 10 per cent of all patients* suffering from thyrotoxicosis and in about 50 per cent of those who show signs of congestive failure The best treatment for this arrhythmia is sub total thyroidectomy Spontaneous return to normal rhythm following operation may be expected in a large percentage of cases

Congestive Failure *In the pre-operative management of congestive* failure the usual measures are employed (Chapter 2) Bed rest restriction of fluid intake relief of pressure caused by accumulation of fluid in serous cavities and the use of mercurial diuretics constitute the measures of greatest value The attempt should be made pre-operatively to control failure since operation in the presence of failure usually means subjecting the patient to an increased risk

If auricular fibrillation does not disappear spontaneously following operation quinidine should be given (page 383) The chances of restoring normal rhythm by the use of this drug are excellent if the usual rules for its administration are followed I do not think that it is of any value to establish quinidine maintenance in thyroid patients following operation after normal rhythm returns for the simple reason that the cause underlying the arrhythmia has been removed Recurrence of fibrillation is rare unless there is also a recurrence of the hyperthyroidism

Pre-operative control of the nervous symptoms is essential The almost specific effect of iodine in calming the pulse rate may likewise cause the

patient to be less apprehensive To fortify its action occasional doses of phenobarbital or chloral hydrate may be used The diet should be made up mainly of carbohydrates and should have a high caloric value because of the increased basal metabolic rate Proteins should not be limited when the serum proteins are low and there is a tendency to edema

The crisis or storm that may occur following thyroidectomy is caused by a severe toxic upheaval or an exaggerated hyperthyroid state Within a few hours after the conclusion of the operation fever tachycardia restlessness sweating nausea or vomiting may appear These symptoms call for prompt treatment It is the common belief that this crisis develops as the result of flooding the system with the internal secretion of the thyroid gland at the time of operation However poor medical preparation of the patient will often predispose to this complication If adequate attention is given to the cardiac condition and to the liver stores of glycogen before operation serious storms may be avoided in most instances although much depends on the judgment of the surgeon in choosing the proper time to operate When the basal metabolism and the pulse rate reach their lowest level following iodine administration the thyroid secretion is being held in the acini and this is the time the surgeon chooses for operation —usually during the second week of pre-operative treatment If the optimum time for operation is allowed to pass toxic signs may appear in spite of treatment and operation at this time increases the risk of crisis The second preparation of the patient after omission of iodine for a time must be carried out but is usually not so successful

Surgical judgment is most important in the prevention of thyroid crisis When the thyrotoxic state is poorly controlled by the medical regime there will be less risk of this postoperative complication if a two-stage operation is performed The anesthetic and the anesthetist are both important Many surgeons prefer local anesthesia but any light anesthesia that permits a liberal amount of oxygen to be available at all times may be used

If a postoperative crisis appears iodine should be given immediately It is usually possible to administer a sufficient quantity by mouth but in emergencies it may be given intravenously The rising temperature should be controlled by ice bags or ice packs Frequent temperature readings are necessary during the period of crisis An oxygen tent is essential but if it is not available the nasal catheter method may be used (page 9?) Oxygen has been found to have a favorable influence on the temperature rise the dyspnea and the cough while the extreme restlessness of the patient should be controlled by sufficient morphine Attention should be paid to the amount of fluids given since the increase in the basal metabolic rate the fever the operation and the anesthetic place a considerable drain on the body stores This need can be supplied together with an essential food substance by giving injections of 500 to 1000 cc of a 5 per cent glucose solution as often as indicated In some cases 5000 cc in 24 hours are required At times reopening the operation wound in the neck and draining

out any serum present may swing the balance in a favorable direction during a postoperative crisis

**Irradiation** of the thyroid as a substitute for operation has been gaining in popularity and is the method of choice in cases where the risk of operation is too great. It may occasionally bring about enough improvement to enable operation to be safely performed at a later date. The same medical preparation of rest and iodine should be employed when treatment by irradiation is used. These courses should be planned and given by a competent radiologist and the results controlled by frequent determinations of the basal metabolic rate.

Roentgen ray therapy is worthy of consideration in the treatment of hyperthyroidism in children. The disease is rare in children under 12 but a number of instances have been reported between the ages of 12 and 15. Since this period of life is important from the endocrine standpoint, Rose and Pendergrass[3] suggest a trial of roentgen ray therapy in order to avoid the necessity of removal of the gland and report their results in 10 cases. In five cases there was disappearance of the goiter and in eight cases recovery was complete. The average dose was 1950 roentgen units over a period of six months. If improvement is not observed in three months, continued use of irradiation is unwarranted. Should exacerbation of the disease occur at any time, the treatment is stopped and the patient prepared for operation.

## ILLUSTRATIVE CASES

### Hyperthyroidism—Death from Edema of the Larynx Following Thyroidectomy—Autopsy

**Case 57** Mrs J B, a colored housewife of 24, was admitted to the Philadelphia General Hospital on 12/29/34 complaining of loss of weight, nervousness and palpitation. The symptoms had been present and progressive for a year.

Physical Examination: B P 140/80. There was a diffuse enlargement of the thyroid, exophthalmos and tremor. A systolic apical murmur was heard and the first sound over the same area was accentuated. There was no increase in cardiac size.

Laboratory Data: Basal metabolic rate plus 39 per cent. The electrocardiogram showed sinus tachycardia. The roentgen examination showed an overactive heart but no enlargement. The blood and urine were negative.

Subsequent Course: Following rather prolonged preparation a subtotal thyroidectomy was performed on 1/24/35. The patient left the operating room in good condition but an hour later developed stridor due to edema of the larynx and died in spite of emergency tracheotomy.

Autopsy (Fig 137): The heart was of normal size and consistency but showed acute dilatation of the right ventricle. No lesions were present.

**Discussion** The development of stridor following thyroidectomy suggests either injury to the recurrent laryngeal nerves or, as shown in this case, edema of the larynx. Hemorrhage into the operative field with pressure on the trachea by a hematoma may cause the symptom. Examination of the larynx should be done at once to determine the cause, and if relief

is not promptly obtained especially if cyanosis develops an immediate tracheotomy is indicated

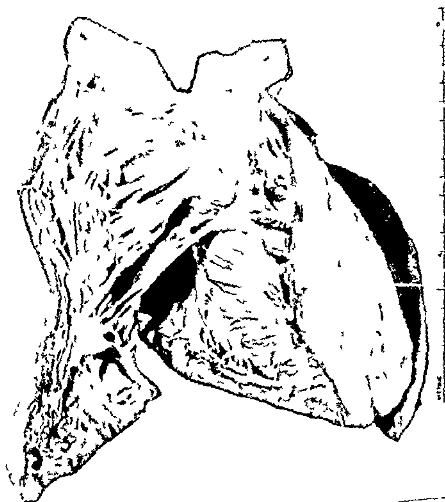


FIG 137 The heart in hyperthyroidism Note absence of hypertrophy and the delicate heart valves (Autopsy No 28 782 Philadelphia General Hospital)

The heart in this case is typical of uncomplicated thyrotoxicosis Note the relative increase in the size of the right ventricle and the normal, delicate heart valves

THYROTOXICOSIS COMPLICATED BY PAROXYSMS OF AURICULAR FLUTTER—COMPLETE RELIEF FOLLOWING SUBTOTAL THYROIDECTOMY

**Case 58** Mrs S B a housewife of 56 was first seen March 1 1936 complaining of loss of weight nervousness and spells of rapid heart action

HISTORY All symptoms began following a series of domestic difficulties six months before the initial examination During this period there was a weight loss of 30 pounds

The patient had previously been treated for a nervous breakdown? When spells of rapid heart action and increase in blood pressure were noted she was diagnosed hyper tensive heart disease and given digitalis in large doses This had no effect She was unable to sleep because of h r nervousness and rapid heart Slight dyspnea was present No edema

PHYSICAL EXAMINATION B P 170/80 Pulse 140 Patient emaciated Skin was warm and moi t much more so than would be expected in a person of her age There was

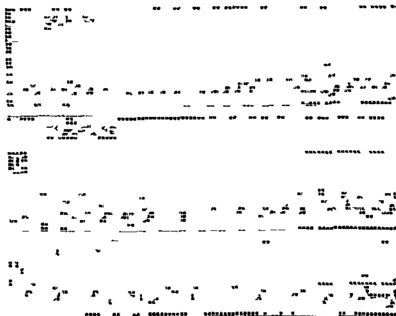


FIG 138 The elect ocardiogram (lead 2) taken on 3/17/36 during one of attacks shows presence of aur cular flutte There are varying degrees of ventricular response A portion of the sam l d of a trac ng tak n eight days later shows sinus tachycard a Note high pointed P av s A record taken at t me of follow up visit eight months fter operat on shows s nus rhythm ate 80 and normal P waves

tremor and sl ght thyroid swell ng No exophthalmos There were pulsat ons noted in the neck and a d ffu apex beat was seen in the m d clavicular l ne There was no card ac enlargement o pe cuss on A syst lic murmur was heard over the mitral area

LABORATORY DATA B M R plus 49 per cent Fluoroscopy showed characteristic ove ct on The is no ncrea e in cardiac size

Th el ctro a diogram (F g 138A) m de at the time of the first examinat on (3/17/36) during a paroxysm of rap d heart act on showed that the mechanism was auricular flutte Th e was a vary ng ventricular re ponse On 3/ 5/36 s nus tachycardia as present Note th ncrease in height of the P waves in the tracing (Lead 2) On 1?/1 / f th lect card ogram was normal

CLINICAL DIAGNO IS A Et olog c Hyperthyro dism B Anatomic No ca diac enlarge ment C Phy iologic Paroxysmal aur cular flutter D Functional Classification Class I Ther peut c Classificat on Class D

DISCUSSION Three weeks later (one week to convince two weeks to prepare) a subtotal thyroidectomy was performed A very small nodule of

thyroid tissue was allowed to remain on each side of the trachea The convalescence was smooth *The paroxysms of auricular flutter did not recur* following operation

On discharge from the hospital on the eighth postoperative day the basal metabolic rate was plus 29 per cent the pulse 100 and normal sinus rhythm was present Potassium iodide was continued in 0 3 Gm (five grains) doses after meals The patient gained three pounds during the first postoperative week

Six weeks later the basal metabolic rate was plus 10 The pulse had dropped to 90 and there was considerable subjective improvement B P 130 90 No cardiac symptoms were present A total gain in weight of 15 pounds since the operation was recorded at this time

Follow up examination three months after operation showed a basal metabolic rate of minus four per cent The weight was now 130 pound a further increase of 15 pounds since the last visit No cardiac symptoms Pulse 80 B P 140 80

When this patient was first seen she was an invalid confined to bed nervous emaciated and discouraged A diagnosis of hypertensive heart disease had been made and her outlook was considered poor The importance of making the correct etiologic diagnosis in heart disease can be appreciated when we view the patient 15 weeks later active quiet and plump restored to health and able to carry on the usual activities of a woman of her years

This result teaches us never to overlook the possibility of thyrotoxicosis in elderly patients who do not present the usual eye signs or thyroid tumor particularly when these patients have increased blood pressure a history of loss of weight nervousness and spells of rapid heart action Here is a curable type of heart disease

### Exophthalmic Goiter—Subtotal Thyroidectomy Followed by Postoperative Hypothyroidism

**Case 59** Mrs G P an Italian housewife of 7 as first seen in October 1935 complaining of *nervousness and palpitation* All the classical signs of thyrotoxicosis were present on physical examination The basal metabolic rate was plus 60

Preparation for operation extended over two weeks and consisted of the usual measures. At the end of this time the basal metabolic rate was plus 35 per cent and the nervous symptoms showed considerable improvement There had been a two pound gain in weight

A subtotal thyroidectomy was performed and the convalescence was uneventful Three months after discharge the patient moved to another city and was lost sight of for three years On November 1938 she returned for study with a diagnosis of chronic nephritis and *secondary anemia There was swelling of the face hand* and legs B P 1 0/80 The heart was slightly enlarged The urine showed a trace of albumin specific gravity 1 0 0 but no casts The basal metabolic rate was minus 40 per cent and the blood cholesterol 285 mg per 100 cc

Discussion The diagnosis of nephritis in this instance was made without a full consideration of the past medical history and was based on insufficient evidence The color the edema and the slight trace of albumin were secondary to the postoperative hypothyroidism and not to a *renal lesion*

The surgeon ordinarily leaves behind a remnant of thyroid tissue the

size of which is governed by his judgment as to the nature of the disturbance evident in the resected gland This glandular substance that remains may support the bodily needs for a time and then burn out and become entirely inactive Consequently a hypothyroid state develops

In some patients who do not complain of any symptoms a postoperative basal metabolic rate a few points below normal is not an indication for thyroid administration However where actual symptoms of myxedema develop treatment with thyroid gland is indicated

This girl is certainly far better off in her present condition than she was when her life was threatened by the hyperthyroidism This fact must be pointed out at the start and unjust criticism directed toward the surgeon should not be allowed The patient should be thankful since this evidence points to final victory over her thyrotoxic state Myxedema is easily managed (page 368)

## Toxic Goiter—Death Following Postoperative Thyrotoxic Crisis—Autopsy

**Case 60** M B a colored female of 48 was admitted to the Philadelphia General Hospital with a chief complaint of nervousnes This symptom was noted a year before and was accompanied by swelling of the neck Following this she developed tremor excessive sweating dyspnea tachycardia and a weight loss of 8 pounds Continuous iodine therapy (five drops t i d ) for the past five months gave some relief

Physical Examination B P 190/90 Exophthalmos thyroid enlargement tremor tachycardia Heart rate 150 rhythm regular apex beat diffuse and wavy in the mid clavicular line The first sound was accentuated at the apex There was a systolic apical murmur A moderate sclerosis of the vessels was observed

Laboratory Data B M R plus 96 to plus 39 Roentgenogram heart overactive but not enlarged Substernal thyroid

Blood count Hemoglobin 8 per cent (Sahli) Red blood cells—4 700 000 White blood cells—6 000 Polymorphonuclears—47 per cent lymphocytes—52 per cent basophiles—1 per cent

Procedure Bed rest iodine sedatives glucose for two weeks When the basal metabolic rate fell to plus 39 per cent and symptoms subsided a subtotal thyroidectomy was performed

Outcome On the first postoperative day the patient was restless and irrational The pulse rate mounted steadily to 170 180 and the temperature to 106 F There was dyspnea Death occurred on the second postoperative day in spite of the usual restorative measures

Autopsy Heart and lungs were removed en masse and are shown in Fig 139 Note the striking prominence of the pulmonary conus and the pulmonary artery The latter was elongated and widened its intrapericardial portion measuring 6 cm in length and the diameter at the base three cm It overshadowed in size the aorta which was likewise somewhat elongated The heart was normal in size with a muscle of firm consistency The valves were normal

**Discussion** Preparation in this case was carried out along the usual lines The postoperative storm that was directly responsible for the death of the patient might have been prevented if a longer period of preparation had been allowed A multiple stage operation might also have averted the postoperative crisis However storms may occur after partial removal or ligation as well as following subtotal thyroidectomy

Iodine is the main drug at the time of postoperative crisis (page 358) The routine use of iodine pre-operatively has removed the main objection

to one stage total thyroidectomy and the risk as shown by figures from many clinics has decreased to less than 1 per cent

Some observers claim that the discharge of adrenalin accounts for the postoperative storm In this respect we can realize how important it is

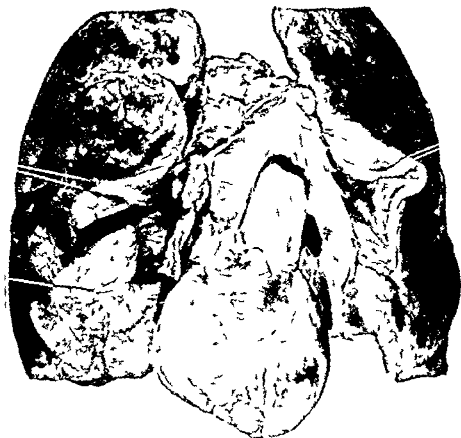


FIG 139 The heart in hyperthyroidism Note the enlargement of the pulmonary artery pulmonary conus and the right ventricle (Autopsy No 9 530 Philadelphia General Hospital )

to save the patient all we can from exposure to disturbing situations before during and following operation Care should likewise be used in prescribing adrenalin for these patients no matter what the situation may be

RHEUMATIC HEART DISEASE WITH SUPERIMPOSED THYROTOXICOSIS—SUDDEN DEATH ON FIFTH POSTOPERATIVE DAY—AUTOPSY

**Case 61** Mrs C H an American housewife of 45 was admitted to the Woman's College Hospital on 9/ 1/34 complaining of palpitation nervousness and weakness of two months duration

History The patient had rheumatic heart disease for some years that required little treatment until two months before admission At this time she noticed increasing nervousness, tremor weakness and palpitation Her dyspnea increased and there was slight edema of the ankles in the evening one month before admission During two months she lost 18 pounds in weight

Physical Examination B P 150 90 Heart rate 120 rhythm totally irregular Tremor Skin warm and moist There was a slight swelling of the right lobe of the thyroid gland The apex beat was palpated in the sixth interspace cm outside the mid clavicular line There was an accentuation of the first sound and a diastolic murmur at the apex The basal metabolic rate was plus 4 The rest of the examination was irrelevant



Fig 140 Eversion of the mitral leaflet

Impression A Etiologic Rheumatic Inactive Thyrotoxicosis B Anatomic Cardiac enlargement Mitral stenosis C Physiologic Auricular fibrillation D Functional Classification Class 3 Therapeutic Classification Class D

Progress On Lugol's solution the pulse rate decreased to 80 but remained irregular The patient was improved No signs of congestive failure were evident A subtotal thyroidectomy was performed on the thirteenth hospital day

The patient's course during the first five postoperative days was stormy She was irrational until the third day On the sixth day because of the continuation of auricular fibrillation she was given a small test dose of quinidine sulfate 0 2 Gm (3 grains) The next day shortly after a second dose of 0 3 Gm (5 grains) was given she died suddenly

Autopsy Heart weight 330 Gm The muscle was pale and soft The left ventricle was dilated The right ventricle was considerably dilated and hypertrophied The left auricle was enormously dilated with thickened and scarred endocardium especially on

the posterior wall On the anterior mitral leaflet there was a thickened fibrotic area This mass of tissue bulged up into the auricle and pressed against the posterior leaflet completely blocking the stenotic mitral orifice (Fig 140) The aortic valve leaflets were thickened puckered and basically incompetent The pulmonary artery was dilated and atheromatous

**Discussion** This patient s death can be attributed to sudden (forward) failure of the circulation resulting from an eversion of the mitral leaflet The cause of this unusual accident remains a mystery Since it followed an attempt to restore normal rhythm by quinidine the situation may be discussed from this angle

It is the usual practice to administer quinidine postoperatively in all cases where auricular fibrillation does not cease spontaneously By the fifth post operative day in over 60 per cent of the cases normal rhythm will replace the fibrillation This patient was given the usual test dose The next day a 5 grain capsule was administered and shortly before the sudden death of the patient the intern had reported the pulse to be regular Sudden death after the use of quinidine in patients with fibrillation of long standing may follow the dislodging of a clot in the auricular appendix with the production of an embolus Consequently the drug should never be used in these cases particularly if there is evidence of congestive failure

In this patient the fibrillation was recent and was brought about by the added burden of the thyrotoxicosis However advanced rheumatic heart disease with mitral stenosis complicated the picture The beginning of coordinated auricular contractions may have created sufficient change in intracardiac pressure to cause the accident The exact mechanism of this rare happening has so far been unexplained

## HYPOTHYROIDISM

Hypothyroidism or myxedema results from a deficiency in the thyroid hormone and is likewise attended by a variety of cardiac manifestations This state may develop in early childhood or in adult life and its effect on the organism in each instance will be quite different Means [60] divides hypothyroid states into (1) infantile myxedema or cretinism (2) childhood or juvenile myxedema and (3) adult myxedema or Gull s disease

### Etiology

**Sporadic cretinism** follows thyroid atrophy but the exact cause of this change is unknown The cretin shows retardation of growth and development associated with delay in bone ossification epiphyseal union and dentition The face is quite characteristic with its stupid expression thick lips and protruding tongue For this reason cretins resemble one another

**Juvenile myxedema** produced when there is lack of thyroid secretion prior to puberty occupies a place between cretinism and myxedema It differs from cretinism since normal or nearly normal amounts of thyroid

secretion are available for the early years of growth and development although the supply is cut off before the process has been completed

**The adult type** of myxedema is a rare disease caused by atrophy of the thyroid gland that develops spontaneously or as the result of a previous inflammatory process This manifestation of hypothyroidism is particularly interesting to us because of the profound circulatory alterations that accompany it The generalized infiltration of skin with a mucus like substance that does not pit on pressure characterizes the condition (see Fig 142A) The myxedema heart is often uniformly enlarged owing to infiltration with the same material Skeletal muscle shows on examination a pale edematous appearance and fluid may collect sometimes in considerable quantities in the serous cavities [9]

### Signs

In myxedema the reduction in the basal metabolic rate is striking Levels of minus 40 and below are not uncommon This decrease is accompanied by profound alterations in the protein metabolism with retention of protein in the intercellular spaces and increase in the proteins and cholesterol of the blood The pulse rate drops the minute volume output decreases and the whole picture is reflected fluoroscopically in the lazy dilated heart of the myxedematous patient The activity of the organism drops very close to the level observed in hibernating animals

### Course

**The onset** of the myxedematous state is slow and marked progress usually takes place before it is detected clinically This may be caused by the gradual destruction of thyroid tissue by some unknown process which may start years before the patient appears for treatment Its nature therefore generally eludes detection

### Symptoms

Symptoms develop in proportion to the reduction in the metabolic rate When this is of slight degree only mild symptoms appear Sweating decreases and the patient ceases to complain of the summer heat * and since the body fires are burning low there is a dislike for the cold weather The myxedematous patient is contented to sit down and take little interest in the passing scene Mental dulness increases and considerable time is consumed by sleep Constipation is complained of and headaches usually appear The hair becomes thin particularly along the back of the neck and deafness may be noted

**The cardiac symptoms** are part of this general picture Dyspnea is first to appear and soon becomes marked on slight exertion Some patients develop cardiac pain that is relieved by the administration of thyroid gland however as Means points out [6f] it is far more common to have thyroid therapy produce angina than relieve it The heart is enlarged the rhythm

* A very suggestive symptom in Philadelphia

regular the rate slow and the sounds are usually feeble If another type of heart disease is already present a superimposed myxedematous state may precipitate congestive failure In spite of these numerous characteristic symptoms *it is surprising how often the diagnosis of myxedema is missed*

TREATMENT

**Thyroid Medication** The effect of thyroid therapy in myxedema is *most gratifying since it restores to normal all bodily processes* Tablets of dried thyroid gland are efficient and less expensive than other preparations Means *has found after a careful study of 50 cases that requirements* show little variation A dose of one half of a grain a day of dried gland should keep the basal metabolic rate of a myxedematous subject at a level of minus 20 One grain daily will maintain it at minus 10 one and one half grains at approximately *minus* 5 and three grains daily at a normal level IT IS OF THE GREATEST IMPORTANCE THAT THE MYXEDEMATOUS STATE SHOULD BE CONTROLLED ON THE SMALLEST DOSES OF THYROID COMPATIBLE WITH A NORMAL EXISTENCE Inasmuch as there is no way of knowing the basal metabolic rate before the onset of myxedema the patient must be regulated by clinical trial and the effect of thyroid therapy on the symptoms closely studied The minimum dosage that gives the desired effect is then continued for the rest of the patient s life

In prescribing or dispensing thyroid tablets the physician should remember that there are differences in the tablets supplied by the various manufacturers and that a patient balanced satisfactorily on one brand may show symptoms of hyperthyroidism on another The figures given above refer to U S P thyroid Variations in the strength of the different preparations will usually be indicated on the label so the necessary adjustments can be made It is however unwise to change the brand of thyroid used Thyroid gland U S P should be prescribed because of its lower cost and the uniformity of its action Familiarity with the dose of this standard preparation is all that is necessary The addition of 1 cc (16 minims) of dilute hydrochloric acid taken with meals may enhance the action of the thyroid gland in the presence of gastric hypo acidity

When thyroid medication is begun there is a latent period of from six *to eight days before its action is evident An elevation in the basal metabolic* rate first appears This is produced by an increase of fat and carbohydrate *metabolism The blood sugar is increased as the glycogen store of the liver* is depleted At the same time sugar tolerance is diminished and glycosuria *may appear* In the usual *subject these changes* may result in a loss of weight If the administration of the thyroid substance is continued restlessness irritability, sweating tachycardia and muscle tremors will be produced

THYROXIN is no more effective than dried thyroid gland This preparation can be administered intravenously but the indication seldom arises The action of thyroid gland by mouth is just as satisfactory and the usual risks that attend any form of intravenous therapy are avoided Thyroxin

administered by mouth is absorbed less uniformly than dried thyroid and consequently for routine use aside from the greater cost it does not display the efficient action of the latter preparation

SEQUELAE Under treatment with thyroid the size of the myxedema heart shrinks the greatest reduction occurring in the largest hearts This is strong proof that the condition is not one of true hypertrophy but rather a manifestation of the myxedematous state Heart size returns to normal slowly as the fluid is eliminated and the tone improves If this does not occur we should search for the presence of another complicating type of heart disease

Care must always be exercised in prescribing thyroid for myxedematous patients for too enthusiastic a start often precipitates grave symptoms Since myxedema favors the development of arteriosclerosis it is not surprising that anginal attacks occur when the basal metabolic rate and consequently the cardiac work are increased to too great an extent in the beginning of the treatment If angina appears the thyroid medication should be temporarily discontinued and when begun again smaller doses should be prescribed

Digitalis has no effect in a case of true myxedema in fact it is poorly tolerated The only indication for its use is the congestive cardiac failure which often occurs when myxedema complicates some other type of heart disease

Some degree of anemia accompanies myxedema and generally can be attributed to the effect of the disease on the blood forming organs When of extreme degree it may accentuate the cardiac symptoms particularly the dyspnea Improvement is then speeded by giving ferrous sulfate 0 6 Gm (10 grains) t i d with the thyroid tablets

## ILLUSTRATIVE CASES

### HYPOTHYROIDISM FOLLOWING IRRADIATION—DEATH FROM CORONARY DISEASE—AUTOPSY

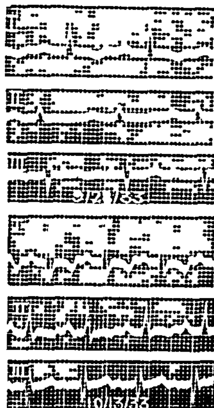
**Case 62** Mrs E K a white housewife of 43 gave a history of hyperthyroidism two years prior to admission to the Philadelphia General Hospital on 8/ 4/33 She received roentgen ray treatment over this entire period Although the nervousness and palpitation were much improved during the last six months she had noticed weakness, dyspnea dryness of the skin loss of hair and swelling of face and legs The skin became thickened and the nails brittle

PHYSICAL EXAMINATION Exophthalmos and widening of the palpebral fissures were present The thyroid was not palpable Rales were present in both lung bases A moderate bilateral pleural effusion was found The heart rate was slow and the sound distant The borders could not be satisfactorily determined because of pleural fluid

LABORATORY DATA Urine showed a cloud of albumin specific gravity 1 010 Blood Hemoglobin 70 per cent (Sahli) Red blood cells 2 800 000 White blood cells 9 000 polymorphonuclears 53 per cent lymphocytes 47 per cent Kahn negative Cholesterol 385 Basal metabolic rate minus 30 per cent. The first electrocardiogram showed low voltage of QRS prolongation of the P R intervals to 0 8 seconds and a left axis deviation Two weeks later (Fig 141A) marked alterations in the T waves appeared and a Q wave in lead 3 was noted

Progress The patient showed very little response to bed rest diuretics and cautious thyroid administration and died suddenly six weeks later

Autopsy Thyroid Considerable fibrosis was present and no thyroid tissue was visible in the section The heart showed hypertrophy of all chambers There was considerable sclerotic thickening of the mitral and aortic valves and extensive atheroma of the aorta





A B

Fig 141 A The electrocardiogram on admission Note bradycardia the low voltage of all waves and the flat T waves A record taken two weeks later following administration of thyroid shows increased voltage The T wave changes were probably caused by alterations in the blood flow to the heart muscle B Atheroma of the aorta associated with hypothyroidism (Autopsy No 26796 Philadelphia General Hospital)

Discussion Myxedema in the adult may be spontaneous or induced The type that follows irradiation or surgical removal of all thyroid tissue (cachexia strumipriva) is much more common today The roentgen ray affects all thyroid cells and if the treatments are continued over a long period may lead to a total suppression of the internal secretion This patient had typical hyperthyroidism two years before admission An excellent result was obtained at the start with irradiation and the treat

ment was continued over a longer period than was necessary with the development of hypothyroidism and later a frank myxedema

High blood cholesterol values are usually obtained in myxedema, and these may be seen to decrease after the administration of thyroid extract The level of the blood cholesterol and the basal metabolic rate vary inversely In non toxic goiter the blood cholesterol is normal while in thyrotoxicosis and thyroid crisis it is low Consequently blood cholesterol determinations are valuable in diagnosis and in following the progress of treatment

This patient s early death from coronary disease the advanced degree of atheroma discovered at autopsy and the high blood-cholesterol value that was associated with her myxedematous state are more than coincidental When the dangers of thyrotoxicosis were avoided she developed the high blood cholesterol which probably speeded up a sclerotic process already present Blumgart has been unable to confirm this view and reports no evidence of rapidly progressing arteriosclerosis among the patients subjected to total thyroid ablation for relief of cardiac pain and congestive heart failure[34]

### Myxedema Complicated by Coronary Arteriosclerosis—Death Following Second Attack of Coronary Thrombosis

**Case 63** N T a bank clerk of 55 was first seen with his physician on November 10 1939 At this time he showed all the typical signs and symptoms of myxedema Two weeks before he had experienced a sudden attack of precordial pain in the middle of the night this persisted for some hours and required a hypodermic injection of morphine for relief

Physical Examination B P 140/80 Pulse 55 There were noted a puffy face sparse eyebrows dry skin and thin hair (Fig 14 A) The heart sounds were distant and soft systolic murmurs were heard over the apex and aortic area The *rhythm* was regular The heart was not enlarged to percussion

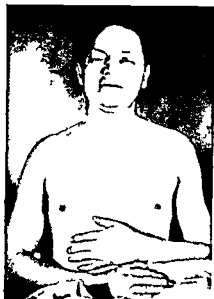
Laboratory Data The electrocardiogram showed low voltage and *in* addition changes that suggested recent coronary occlusion (Fig 14 C) The roentgenogram showed slight cardiac enlargement (Fig 14 B) The blood cholesterol was 370 *mg* The blood count was normal urine and Wassermann negative The basal metabolic rate was *minus* 4

Clinical Diagnosis A Fuolog c Myxedema B Anatomic Coronary sclerosis *Coronary occlusion* Cardiac infarction C Physiolomc Sinus bradycardia D Functional Classification Class 4 Therapeutic Classification Class E

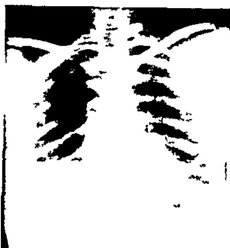
Discussion Means[46] believes that the occurrence of coronary thrombosis *in* myxedema is largely an accidental association He states that persons who develop myxedema usually do so in the age periods when coronary thrombosis is also common and he is not surprised that certain patients should have both diseases

Some of the patients with myxedema have angina before thyroid treatment is begun Others are free of pain until thyroid medication is pushed too fast for the caliber of the coronaries and then seizures develop The treatment in these cases consists in balancing the amount of daily thyroid ration to give the greatest relief from the symptoms of myxedema without aggravating the angina Many times this dose will be under one

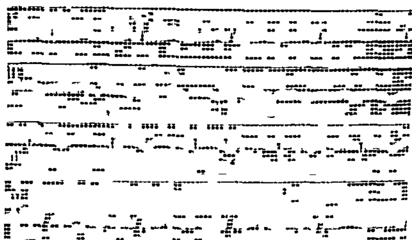
grain of thyroid gland a day Nitroglycerine should be given as often as needed to control the angina



A



B



C

Fig 142 A Myxedema B Roentgenogram shows slight cardiac enlargement C The electrocardiogram in myxedema Note the low voltage of all waves The S T intervals in leads 2 and 3 show doming that is quite suggestive of old posterior coronary occlusion Lead 4F is normal except for low voltage

The association of arteriosclerosis with myxedema cannot fail to call to mind the relationship between diabetes and similar changes in the

coronary tree In both diabetes and myxedema arteriosclerosis is an early complication and acute coronary occlusion often terminates the picture in each instance Joslin believes that the problem of arteriosclerosis in diabetes will be solved if complete oxidation of fat is accomplished High cholesterol values are found constantly in diabetes as well as in myxedema With such a large cholesterol supply available in the blood stream it is natural that investigators should conclude that this substance finds its way into the vessel walls and becomes concentrated in the spots where necrosis develops Further support is given to this view by laboratory workers who have fed diets high in cholesterol to animals with the production of similar lesions

Whether or not we make use of this experimental data in the management of our diabetic and myxedematous patients we must admit that many problems (and secrets) physiologic biologic and pathologic are closely linked to that fascinating chemical compound, cholesterol

# 12

# CARDIAC ARRHYTHMIAS

Intelligent pulse palpation is an invaluable short cut to a great deal of information essential to the management of the cardiac patient More over there are important inferences which the pulse and only the pulse *enable us to draw While the rate size and compressibility of the pulse are* important notations rhythm deserves the most careful appraisal Attention to a few fundamental rules and constant practice should enable every physician to diagnose the majority of the arrhythmias clinically especially when pulse palpation is combined with careful auscultation of the heart Needless to say this is a great advantage in emergencies when the electro cardiograph is not available

We can no longer state that the rhythm of the heart is irregular or slightly irregular The type of the arrhythmia should be put down for it can be determined with very little difficulty by the general practitioner at the bedside In fact much of our present knowledge of the cardiac irregularities is a heritage from a country doctor since the greatest part of the contributions of Sir James Mackenzie were made while he was in general practice at Burnley Instruments of precision were perfected by him to test his theories but when the many problems surrounding the arrhythmias were solved he discarded the instruments and returned to continue his investigations at the bedside of the patient

Irregularities in the rhythm are present many time in the absence of heart disease However the impression they make on the nervous system of the patient gives them a place of importance when treatment is planned The patient whose nervous system is receptive to the stimuli of these abnormal beats is usually the patient who is constantly engaged in the palpation of the radial pulse Consequently a harmless arrhythmia may be the starting point of a neurosis that eventually leads to as much ill health as an organic lesion

A clear understanding of the arrhythmias comes with a thorough knowl edge of the physiology of the cardiac mechanism (Chapter 24) Abnor *malities of the cardiac action arise when the rate of impulse production i* increased or decreased when the impul e has its origin outside the regular sinus node or when disease processes block the normal distribution of the impulse Before considering the treatment of the cardiac irregularities separately, a few general rules that may prove useful in their recognition will be mentioned

## DIAGNOSIS

**Age Relations** If an arrhythmia is present in a child under eight years of age it is almost certainly sinus arrhythmia Heart block caused by a congenital defect in the septum may be noted at birth but it is rare (page 343) Auricular fibrillation is seldom present to complicate rheumatic or congenital lesions in the very young unless cardiac failure is imminent (page 348)

**The cardiac rate** is an important consideration in the diagnosis of any arrhythmia Persisting and regular ventricular rates below 40 point to complete heart block When a pulse rate over 140 suddenly appears in a patient at rest and continues at this level or higher for a space of hours to return suddenly to normal a paroxysm of tachycardia or flutter is usually the mechanism Pressure over the carotid sinus in the neck serves to differentiate since it causes marked slowing in the ventricular rate if flutter is present while if it has any effect at all on a paroxysm of tachycardia it will stop it at once and the pulse rate returns suddenly to normal

**Premature Beats vs Auricular Fibrillation** If the heart's rhythm is irregular with a slow ventricular rate it will require careful auscultation to differentiate between frequently recurring premature beats and auricular fibrillation If the patient is exercised or given an inhalation of amyl nitrite to speed up the pulse the differentiation is easy With auricular fibrillation the irregularity of the heart becomes more pronounced while in the presence of premature contractions the rhythm becomes rapid and entirely regular It is unusual for premature beats to persist with pulse rates above 110

**Alternation of the pulse** is a very important type of arrhythmia to diagnose because of the bearing it usually has on prognosis Pulse palpation may suggest its presence but it may be more readily demonstrated by using the sphygmomanometer (page 409)

**A skipped or dropped beat** at the wrist may be caused by premature contractions heart block or sinus arrest The last two are rare By listening over the precordium while palpating the carotid pulse the sound of the premature beat may be detected while precordial auscultation in patients who have heart block or sinus arrest reveals no extra sound during the pause An electrocardiographic examination may be necessary to distinguish between heart block with dropped beats and sinus arrest although in the presence of the former various signs that point to cardiac disease viz enlargement of the heart fever of a rheumatic process etc may be evident Sinus arrest is more likely to occur in healthy hearts while heart block never does

**Bundle branch block** may be suspected when a splitting of the first heart sound occurs in the presence of other evidences of cardiac disease

It is usually caused in these instances by asynchronous contraction of the ventricles

The symptoms that accompany the cardiac arrhythmias vary from the nervousness of the patient who experiences occasional premature beats to the coma and convulsions that are often seen in patients suffering from varying degrees of A V heart block The same irregularity in one person may cause no symptoms at all in the second Even marked disturbances of cardiac rhythm such as auricular fibrillation may be unappreciated by the nervous systems of some individuals while infrequent premature beats in susceptible patients may be accurately catalogued as to number and time of day of their occurrence

In all cases it is important to secure a detailed description of the type of irregularity causing the disturbance Many patients will give a description so characteristic that a diagnosis can be made on the history The sensations described as *skippings* *pulsations* *heart turning over* '*chokings* are nearly always due to premature beats Sudden racings and flutterings are terms generally used to refer to paroxysms of rapid heart action

Occasionally the sudden onset of a paroxysm of tachycardia may prove more than the myocardium of an elderly patient can stand in which event the symptoms of congestive cardiac failure may quickly appear The situation precipitated by the arrhythmia then assumes the nature of a medical emergency

Regardless of the type of irregularity complained of the final judgment in each case should rest on the result of complete physical examination Particular attention should be given to the blood pressure and the attempt should be made to demonstrate the presence of pulsus alternans if the clinical findings warrant the search The jugular bulb should receive close attention and study Many times the waves observed here reflect a type of auricular activity that permits definite conclusions to be made in regard to the nature of the arrhythmia Careful precordial auscultation should be made during pulse palpation Carotid sinus pressure should always be practiced and its effect on the irregularity noted A careful evaluation of all the signs and symptoms of cardiac disease is always the deciding factor in estimating the importance of any arrhythmia and in planning management

## SINUS MECHANISMS

### Sinus Tachycardia

**Case 64** M R a physician of 9 came to the hospital for a cardiac study because of tachycardia of three weeks duration The average rate was 110 onset and offset were gradual

Physical Examination B P 108/70 The heart was not enlarged No murmurs were heard The electrocardiogram that the patient requested revealed only a sinus tachycardia with a rate of 1 0 Further study however showed a temperature of 99 3 F and an active tuberculous lesion at the right apex of the lung

**Discussion** The heart many times gives warning of trouble in a neighboring organ This case history shows how dangerous it is to confine an examination to one region or organ of the body The sinus tachycardia here interpreted as heart disease was the result of the toxemia and fever of an active tuberculosis

Sinus tachycardia is likewise commonly produced by overindulgence in tea coffee tobacco and alcohol gastro-intestinal tract disturbances hemorrhage shock hyperthyroidism and cardiac failure The tachycardia of the latter condition is controlled by the regime described for congestive failure

## Sinus Arrest

**Case 65** Miss E J a student of 17 was referred to the Cardiac Clinic of the Woman s College Hospital by a school physician because of a slow irregular pulse Rate 48 Occasionally dropped beats were palpated at the wrist No precordial sound was heard on auscultation during the pauses Cardiovascular symptoms were absent and the past history was negative for rheumatic infection The physical examination except for the slow pulse and arrhythmia was entirely negative

Clinical Diagnosis Possible heart disease (patient with signs referable to the heart but in whom diagnosis of cardiac disease is uncertain) Functional Classification Class I Therapeutic Classification Class A Electrocardiogram needed to establish the diagnosis

**Discussion** The electrocardiogram showed the presence of sinus arrest (See Fig 180A) This girl was active in all forms of athletic activity and at the time of the examination was engaged in a school hockey tournament It is not uncommon for well trained athletes to show these manifestations of an increase in vagal tone consequently in this patient the bradycardia and sinus arrest were disregarded The latter disappeared when tincture of belladonna was administered in full dosage over the course of one week No treatment of course was indicated A follow up examination in three months showed that the sinus arrest had disappeared

## Sinus Arrest During the Course of Arteriosclerotic Heart Disease

**Case 66** R S a retired policeman of 67 was admitted to the Woman s College Hospital on 1/3/31 complaining of a sudden severe chest pain The pulse was 40 and the rhythm irregular

Physical Examination B P 100/70 T 99 2 Pallor and sweating were observed Circulatory balance was quickly gained but the pulse remained slow and irregular No precordial friction rub appeared

Laboratory Data The orthodiagram was normal Blood count normal Urinalysis negative Blood Wassermann negative

Electrocardiogram (see Fig 180B) sinus arrest

Clinical Diagnosis A Etiologic Arteriosclerosis B Anatomic Coronary sclerosis Coronary occlusion (?) C Physiologic Sinus arrest D Functional Classification Class 4 Therapeutic Classification Class E

**Discussion** The slow pulse accompanying the sudden onset of chest pain suggested at first a posterior coronary occlusion but an electrocardiogram showed the presence of sinus arrest instead of the expected complete A V block This suggested that the artery supplying the sinus node was

the site of the lesion No signs of circulatory insufficiency attended the slow pulse rate and the treatment of this patient was the treatment of the coronary disease The rhythm returned to normal in one week and no irregularities were noted during the remainder of the patient s period of convalescence

This patient was seen again five years later when he was admitted because of a urinary tract obstruction secondary to prostatic hypertrophy and cardiac studies were repeated The sinus arrest was no longer in evidence but there was prolongation of the P R intervals to 0 24 second and a small Q wave in lead I The orthodiagram again showed no cardiac enlargement Routine physical examination on the second visit revealed a large pulsating abdominal mass proved by roentgen study to be an aneurysm of the abdominal aorta In spite of these evidences of wide spread sclerosis a prostatectomy was successfully performed and convalescence was smooth At a follow up examination two years after the prostatectomy the patient was ambulatory and his only complaint was a mild angina on effort

Sinus arrest in Case 65 was allied to vagal stimulation and sinus arrhythmia in a healthy heart and we may assume that it was a transient functional alteration However in Case 66 the disorder is most likely associated with a deficiency in the coronary circulation Since some degree of A V block was also present there were likewise some circulatory changes in the region of the bundle The vertigo complained of by the patient on his first admission was probably caused by the cerebral anemia that followed the sinus arrest The occasional dropping of a single beat will rarely produce any subjective disturbance other than palpitation in patients who are sensitive to alterations in their cardiac action In occasional cases the blocking in succession of two three or more beats may cause symptoms of faintness or even syncope to appear and the resemblance to Adams Stokes attacks will be very close In patients who complain of occasional fainting spells in the absence of signs of disease in the nervous system or heart sinus arrest must be considered as a possibility

## Sinus Bradycardia Caused by Hypersensitive Carotid Sinus

**Case 67** R F a male executive of 50 was admitted to the Woman s College Hospital on 7/15 36 for study because of vertigo and faintness of a year s duration Two attacks of syncope occurred while at work the week before admission The periods of unconsciousness were brief neither exceeding two minutes, and there were no convulsive movements Each attack was attended by an extremely slow radial pulse (50 to 60) The physical examination of the chest was entirely negative An orthodiagram showed a heart well within the limits of normal in size and shape The electrocardiogram (see Fig 196) showed bradycardia and wandering pacemaker A G I tract examination showed a moderate degree of visceroptosis

**Discussion** A marked sinus bradycardia was present in this case associated with obesity and hypotension Pressure over the carotid sinus on the right slowed the heart rate and caused faintness In 1927 Herring showed that this phenomenon was caused by a reflex from the carotid

sinus a slight swelling at the bifurcation of the common carotid artery at the upper level of the thyroid cartilage The sinus nerve taking its origin in the wall of the carotid sinus is the afferent reflex pathway It joins the glossopharyngeal nerve Irritation of the wall of the carotid sinus causes two reflexes the first produces slowing of the heart while the second causes a fall in the blood pressure The impulses to the heart that bring about the slowing are carried by the vagus nerve

While this patient was in the hospital it was discovered that both attacks of syncope occurred on sultry days when a very closely fitting stiff collar had been worn Inquiry revealed that there had been a considerable gain in weight during the past year and larger collars had not been purchased The patient was accordingly advised to wear a soft type of collar A weight reduction program was advised Large doses of thiamin chloride were prescribed since recent studies have suggested that deficiency states induced by insufficient vitamin $B_1$ are often attended by hyperexcitability of the carotid sinus reflex An abdominal belt was ordered and the patient was given capsules containing 25 mg (3/8 grain) of ephedrine sulfate to be taken as needed for vertigo A year later this man reported no recurrence of the syncopal attacks and a weight loss of 10 pounds

Females seem to be less subject to hyperexcitability of the carotid sinus reflex than males[408] Local disease processes most of them arteriosclerotic in nature may produce excessive sensitiveness of this reflex arc by a lowering of the threshold of irritability In some cases where the simpler measures outlined above are not effective in preventing attacks of syncope a denervation of the carotid sinus is to be considered I have seen several cases similar to the one whose history is outlined here but have never been forced to advise surgical relief for the condition

This patient s bradycardia persisted and an average pulse rate of 55 was noted on many occasions subsequently A slow pulse may have no significance particularly in adults who have a hypersthenic build while on the other hand it may serve to attract attention to a serious cardiac defect for example heart block auricular fibrillation or flutter Flutter accompanied by a high degree of block may produce a slow ventricular rate Auricular fibrillation likewise may have a high degree of block which will result in a slow pulse although if carefully studied the pulse will also be found to be irregular

Abnormalities in the formation or conduction of the cardiac impulse may produce a slow pulse Sinus arrest as we have just seen is an example of this kind The pulse may be slow in partial or complete heart block

Certain toxic states may be responsible for bradycardia For example it is often produced by the action of digitalis and it frequently accompanies icterus Following certain infections notably typhoid fever and influenza bradycardia may appear and be quite pronounced The severe toxic state accompanying uremia also produces a slowing of the pulse Intracranial lesions like tumor hemorrhage or concussion commonly cause sinus bradycardia

Bradycardia is frequently met in hypothyroidism or myxedematous states consequently a determination of the basal metabolic rate is indicated in patients who have bradycardia and suggestive clinical findings The low metabolic rate is responsible for the slow pulse rate, both show an increase when thyroid extract is given Finally a slow pulse may be present in patients with aortic stenosis Here a physical examination of the heart serves to differentiate

The management of bradycardia depends upon the cause A slow heart is not necessarily an inefficient heart since many times in cases of complete *heart block the patient can carry on for years with a pulse rate that* is constantly between 30 and 40

### Sinus Arrhythmia

**Case 68** Master R S age six was referred to the Cardiac Clinic of the Woman's College Hospital because of an irregularity of the cardiac rhythm coming on shortly after a tonsillectomy There were no symptoms referable to the heart No murmurs were present and an orthodiagram showed the heart to be well within the limits of normal in size and shape The electrocardiogram (see Fig 194) showed the pulse irregularity to be due to sinus arrhythmia

**Discussion** Sinus arrhythmia following alterations in the vagal tone is the most common irregularity in children Mackenzie referred to it as the youthful type of irregularity Occasionally the condition may be so marked that unless the patient is carefully examined fibrillation may be suspected Sinus arrhythmia may be recognized by noting its relationship to the different phases of respiration It is abolished by atropine which paralyzes the vagal endings in the heart and produces a more rapid regular heart rate Sinus arrhythmia is physiologic, and no treatment of course is required

## PREMATURE CONTRACTIONS (EXTRASYSTOLES)

The occasional occurrence of extrasystoles is compatible with a long and healthy life After 50 they are as insignificant as gray hairs, and if the rest of the examination of the cardiovascular apparatus is negative they should be disregarded Extrasystoles arise from impulses generated outside the sinus node acting on the heart muscle after the refractory period is ended but before the arrival of the next impulse from the pacemaker These beats are easily recognized clinically by noting the occasional intermission in the radial pulse at the same time ausculting over the precordium where the extra beat will be heard

The *premature beat is generally a weaker beat* following the regular contraction It is weak because it occurs at so short an interval after the normal beat allowing the ventricle less than the usual time for filling The output of the heart following the premature beat is less for the same reason in fact some beats may be so weak that the aortic valves do not open The compensatory pause gives ample time for ventricular filling consequently the next beat is stronger than normal and this directs the patient's

attention to the heart and accounts for the complaints of "thumping in the chest," "choking," etc.

### Origin

Premature beats may originate in any part of the heart: the auricular muscle, the ventricular muscle or the A V nodal tissues. They may occur at any age from a number of intrinsic and extrinsic causes ranging from a cup of coffee to a coronary occlusion. Usually it may be said that the younger the patient, the more infrequent is this form of arrhythmia and when it does occur the more likely it is to arise from actual myocardial disease.

**Auricular premature contractions** can usually be distinguished from those of ventricular origin by the compensatory pause. In ventricular premature beats the pause is fully compensatory; if the beat is auricular or nodal the pause is not compensatory.

Premature beats may occur infrequently in some patients, in which event their recognition is easy. In other patients many premature beats may occur in the course of a minute; in these cases the irregular rhythm may closely simulate auricular fibrillation. Premature beats may occur after each normal beat (pulsus bigeminus) or after each second normal beat (pulsus trigeminus). In rare instances the premature beat may occur between two normal beats without altering the basic rhythm (See Fig 201A). The latter is known as an interpolated beat. Here the term, "extra systole," may be correctly applied.

## ILLUSTRATIVE CASES

### Post traumatic Cardiac Neurosis—Significance of Multiple Premature Contractions

**Case 69** Miss E F, a typist of 40, complained of frequent "pulse skippings" following hospitalization for injuries caused by an automobile accident. Examination showed a blood pressure of 140/80, frequent premature beats, no murmurs and no cardiac enlargement. The Wassermann and other laboratory examinations were negative. The periods were scant before the accident and following the accident the menses were absent.

**Discussion** The discovery of the presence of the premature beats by this patient following an automobile accident was (to use her own words) "a terrifying experience." When first examined all the chest sensations that usually accompany these interruptions in the cardiac rhythm were described in detail. At each subsequent visit the patient brought a detailed record that demonstrated at least an increasing skill in pulse palpation.

The age, mannerisms, menstrual history, physical examination, type of cardiac irregularity and voluminous charts made of the "skippings" all suggested the functional nature of the cardiac complaint in this patient. Treatment was begun by frankly telling her that no evidence of any

heart disease could be detected outside of the irregularity The premature beats were recorded and the tracing was shown to the patient while the many factors operative in producing them in her case were reviewed She was instructed not to palpate her radial pulse to avoid fatigue, and to get more rest at night To this end she was given a tablet of sodium bromide 1 0 Gm (15 grains) in water after meals Tobacco tea coffee and alcohol were eliminated

The premature beats became much less noticeable and annoying after a week on this regime although examination showed that they were still present At this stage in the treatment the patient was advised to get more out-of-door exercise She chose walks in the country and was not long in noticing that exertion caused the premature beats to disappear The walks were beneficial and she began to sleep better at night and when she was next seen at the end of two weeks improvement was reported A final help was given to her at this time in the form of a capsule of quinidine sulfate 120 mg (2 grains) when it was determined that no reaction followed the initial dose of this drug She was instructed to take one or two of these capsules when the premature beats became annoying during working hour

Search for foci of infection is most important in the management of patients of this type It must not be forgotten that an infected gallbladder can cause these disorders of rhythm which promptly disappear following operation in many instances (Chapter 17)

The relationship between the accident and the onset of the extrasystoles in this patient has medicolegal significance since it brings up the subject of cardiac trauma (page 486) We must admit however that here the stage was set for the occurrence of the premature beats before the accident and trauma should only be viewed as another provoking factor Extrasystoles may follow cardiac injury but they may also occur in the absence of any myocardial damage Their occurrence in this case is by no means proof in itself of damage to the cardiac structure by the accident

### Premature Ventricular Contractions Associated with Hypertensive Heart Disease

**Case 70** Mrs R E a housewife of 60 when first seen complained chiefly of palpitation caused by frequent irregularities in cardiac action The patient was overweight showed an elevation of the blood pressure (190 110) cardiac enlargement of the hypertensive type a systolic apical murmur and beginning congestive cardiac failure The electrocardiogram is shown in Fig 01B

**Discussion** The premature beats also comprised the chief complaint of this patient but examination showed the presence of cardiac damage They were successfully treated by rest and slow digitalization Elixir of phenobarbital (N F ) in 5 cc doses after meals was given for a few days to decrease the apprehension of the patient while measures were instituted for the control of the congestive failure by digitalis With improvement in the circulatory status the premature beats disappeared

# THE PAROXYSMAL TACHYCARDIAS

## A-V Nodal Paroxysmal Tachycardia in the Absence of Other Evidence of Heart Disease

**Case 71.** E. W., a sales executive of 37, was first seen in November, 1934, complaining of attacks of rapid heart action. The rate averaged 150 per minute; the onset and offset were abrupt and attacks were usually associated with some digestive disturbance. Physical examination showed no cardiac enlargement, no murmurs and a normal blood pressure. The past medical history was negative except for hay fever. Wassermann negative. *The electrocardiogram showed auriculoventricular nodal tachycardia* (Fig. 206A).

**Discussion.** Paroxysmal tachycardia, first described by Cotton in 1867, is caused by a succession of premature beats or extrasystoles emanating from a focus in the auricle, the A-V node or the ventricle. It is a rare arrhythmia, occurring only 17 times in 3000 consecutive electrocardiograms at the Woman's College Hospital. Of these, five were of the auricular variety, nine of the nodal and three of the ventricular. The auricular and nodal paroxysms occurred in ambulatory clinic patients, while the ventricular forms were present in ward patients exhibiting signs of advanced heart disease.

In most patients who have the supraventricular types of tachycardia no heart disease can be demonstrated, although in some well-compensated rheumatic or arteriosclerotic lesions may be present. Occasionally the paroxysms are associated with toxic foci, particularly in the gall bladder, the elimination of which may *be the master stroke in therapy*. *In patients* with varying degree of A-V block, a prefibrillary type of ventricular tachycardia may be observed during Adams-Stokes seizures (page 618). Ventricular tachycardia may occur as a sign of the toxic action of digitalis.

This patient gave a history of attacks of rapid heart action for a period of years, but when their frequency increased he became alarmed and came to the hospital for study. The fact that he had no other evidence of cardiac disease was first established. The roentgen findings were negative and the electrocardiogram following a seizure (See Fig. 206B) was likewise within the limits of normal. During his short stay in the hospital many attacks were observed. Some were readily controlled by vagus or carotid sinus pressure; others showed a tendency to resist all treatment for hours.

*A striking fact in the past history* of this patient was the presence of seasonal hay fever beginning about August fifteenth of each year. Paroxysms were more frequent at this time but also occurred at other seasons of the year. A history of allergy in these cases warrants a complete study (Chapter 16).

**Quinidine.** One of the most reliable remedies when the paroxysms tend to be prolonged in the absence of organic heart disease is quinidine sulfate, the dextrorotary *isomer of quinine*. Wenckebach *in 1917 first noted that* quinine in malarial patients often abolished an existing fibrillation of the auricles, while in 1918 Frey found that quinidine possessed the same gen-

eral actions as quinine but exhibited a more intense and selective action on the heart

Quinidine sulfate is a very soluble drug and is rapidly absorbed from the gastro-intestinal tract its action becoming manifest about 20 minutes after administration It is likewise rapidly eliminated a fact which has a direct bearing on the amount and frequency of the prescribed dose

Quinidine lengthens the refractory period of the cardiac muscle and depresses the conduction rate Consequently the drug does not cure disease—it merely smooths out the cardiac action and enables the normal *pacemaker in the sinus node to gain control of the rhythm Quinidine is* therefore useful in paroxysmal tachycardias extrasystoles auricular flutter and in certain selected cases of auricular fibrillation It is most satisfactory in its action when the heart is otherwise sound or the damage if present, is not extreme

Quinidine is best administered in capsule form It is most important to give a test dose of 0 2 Gm (3 grains) of the drug a few hours before therapy is begun unless the emergency is extreme This initial or test dose *in some cases may prove sufficient to abolish the paroxysm* If not in four hours a 0 3 Gm (5 grains) capsule may be given and continued at this interval during the next 24 hours If toxic signs do not appear and the paroxysm persists the dose may be doubled and given at the same interval the next day

Gastro-intestinal tract symptoms may be the first manifestations of untoward effects of quinidine nausea vomiting or diarrhea appear early in some cases Fulness in the head followed by headache, vertigo ringing in the ears and in rare cases deafness are symptoms occasionally seen in some patients in such circumstances the drug should be withdrawn Toxic cardiac symptoms consisting of short runs of tachycardia frequent premature beats or intraventricular block are rare Respiratory distress has been observed to follow large doses Cutaneous eruptions urticarial petechial or scarlatinal in nature have been reported Embolism has followed the ill advised use of quinidine in cases of advanced mitral stenosis in the presence of some degree of congestive failure This complication of quinidine therapy is discussed in connection with the treatment of auricular fibrillation (page 394)

Occasionally quinidine sulfate may be given intravenously if the emergency is extreme in doses of 0 2 to 0 4 Gm dissolved in 30 to 60 cc of physiological saline Some brilliant results have been reported following its administration by this route, but I have never had to resort to it It is almost always possible to give quinidine by mouth in the treatment of paroxysmal tachycardias of auricular or nodal origin

Quinidine sulfate 0 3 Gm (5 grains) every four hours was sufficient to curtail temporarily the paroxysm in this patient We were very *much* interested in him, and when he left the hospital a few days later he was requested to keep in touch with us and continue the quinidine as a prophylactic measure until he could arrange the time for a more extended

investigation Consequently on his journeys he kept us well informed Communications came from various sections of the country and reflected the attempts made to meet the question of therapy in paroxysmal tachy cardia They were written by a patient of high intelligence and I believe the details reported in them to be accurate Therefore I am including the following excerpts unchanged

> Boston Mass
> November 7 1934
>
> When I left the College Hospital I took a train for Boston Toward morning I had a very severe attack and could not con tinue at work that day so I went to Dr —— who put electrodes on me again (I am getting used to them by this time) and then gave me two teaspoonsful of wine of ipecac This stopped the attack all right but I vomited for 24 hours I do not feel as if I *have any stomach left Perhaps the purpose of this treatment* was to get rid of my stomach and drop my heart down in its place in the hope that it would behave better amid unaccustomed sur roundings Seriously I would rather have the tachycardia as you call it than vomit my —— head off

The production of vomiting is a most effective way to end an attack Putting the finger down the throat to induce gagging often suffices Apomorphine has been suggested for the same reason In this instance the ipecac was effective when carotid sinus pre sure failed The patient s opinion expressed so frankly in the above letter must always be respected before repeating this remedy in the same dosage

> Buffalo N Y
> November 29 1934
>
> I was fairly well after my vomiting stopped and was able to get some work done I took one of your capsules (quinidine sulfate) after each meal In a week my ears began to ring and when I could stand it no longer I went to see an ear specialist in this city who told me the nerve of hearing had been perma nently damaged by the medicine I was taking and advised me to stop it However the ringing continued (It s Armistice Day every day with me) and two days ago I had another attack

The onset of cinchonism was a real indication for the withdrawal of the quinidine Tinnitus and sometimes deafness following quinidine therapy are not uncommon and may appear as in this case at a later date follo ing prolonged administration A drug idiosyncrasy might be expected in an individual of this type although permanent harm rarely results from the use of quinidine Relief has followed cessation of the medication in patients that I have seen Certainly continuous quinidine therapy is not to be recommended for those patients whose attacks occur at long intervals In cases like the one under discussion however I think that it was indicated

because of the frequency of the seizures and the amount of disability they caused

> Chicago Ill
> December 1 1934
>
> The radio business is improving but last week after working for two days straight I had another bad attack When the eye pressure and the neck hocus pocus failed again I did not have the nerve to start up the vomiting so went to see an M D in this city I told him that I had to have relief from the spell and he said that he would use a new drug that would stop it right away It did but let me say that it was some experience! I was given an injection in the arm and in about two minutes I was as red as a lobster and could hardly get my breath I thought that my last hour had arrived and although there is nothing at all unusual about dying in Chicago it seemed a horrible way to meet my end

The new drug mentioned by our trusting traveler was most certainly acetyl beta methylcholin chloride (mecholyl) Popularized by Starr and his workers it has been used in the treatment of the paroxysmal tachycardias since 1933 It is effective on subcutaneous injection in doses ranging from 20 mg (1/3 grain) to 40 mg (2/3 grain) depending on the age and weight of the patient Under 20 years of age an initial dose of 10 mg (1/6 grain) should be sufficient to terminate the attack Obese patients usually require the maximum dosage If the attack continues for a minute after the appearance of the flush described in the above letter (so characteristic of the drug) the site of the injection should be massaged to hasten absorption If this is ineffective the stimulation of the carotid sinus should be tried again for this procedure is sometimes successful if repeated after injection of mecholyl The drug may be given orally in 60 mg to 1 0 Gm (1 to 15 grains) doses which are followed by a slower and milder action and the flushing may fail to appear

Mecholyl occurs as fine white crystals which are hygroscopic and freely soluble in water The solution is stable to heat and has a bitter taste Mecholyl was discovered when search was made for a choline derivative more suitable for clinical use than acetylcholine and lacking its nicotine like action Choline and acetylcholine have been known for many years and recently it has been shown that acetylcholine is the actual chemical substance released in the muscles when parasympathetic nerves are stimulated

Mecholyl lowers the blood pressure slows the cardiac rate causes constriction of the bronchioles (accounting for the asthma) stimulates the sweat glands increases peristalsis, and dilates the peripheral blood vessels Its action in stimulating the parasympathetic nerves may be described a antagonistic to adrenalin The possibility of making to order other similar drugs possessing a variety of such selective actions upon the various nerves

and ganglia of the human body suggests a busy future for the therapeutic engineers

Because of the untoward effects that are sometimes produced by mecholyl a hypodermic syringe containing atropine sulfate 1 mg (1/60 grain) should be kept handy whenever the drug is used Atropine abolishes the effect of mecholyl and in emergencies may be used intravenously The side effects of mecholyl such as salivation sweating and general discom fort Starr considers to be more than compensated for by the relief from the attack I consider them so disturbing that I reserve mecholyl until all other measures to terminate an attack have failed When the prolonged rapid heart rates seriously affect myocardial function I have used mecholyl Each time I have been forced to follow with atropine (page 457)

Mecholyl may cause the inversion of the T wave of the electrocardiogram in some patients When successfully used for an attack of paroxysmal tachycardia the transition from the abnormal rhythm to sinus rhythm is seen This transition may be attended by prolonged conduction short periods of asystole and premature contractions The same effects can be produced by vagal stimulation

Bloom and Cashon[33] observed a very severe reaction following the intravenous injection of 10 mg (1/6 grain) of mecholyl used to stop a paroxysm of auricular flutter Normal rhythm was restored following the appearance of heart block and ventricular tachycardia but they nearly lost their patient Mecholyl should never be used intravenously In cases of ordinary paroxysms that give a previous history of spontaneous cessa tion where the patient is young and the myocardium in good condition mecholyl should not be used

Let us return from this digression to the recorded experiences of this interesting patient

Los Angeles Cal
February 5 1935

I am sorry not to have written to you before this but have been busy here—in the rain Since it received its volley in Chicago my heart behaved pretty well until two weeks ago After several flare ups I went to an M D in this city and now you will have the real diagnosis! I have a form of intoxication arising in my intestinal tract This doctor has actually visualized the inhabi tants and my flora are far from correct There are twice as many germs of one kind present The effect of this inequality in the population in this sector is reflected in my cardiac kick ups I am taking irrigations three times a week for the colon and quantities of a special kind of milk that is charged with reinforcements for the germs that are losing the battle for me Soon all will be right again By the time it stops raining I expect to be cured

Our patient at this stage seems to be in an optimistic mood At least the therapy now seems to be directed toward trying to discover the cause of

the attacks of paroxysmal tachycardia instead of seeking new remedies to abolish individual seizures The presence of hay fever and the occurrence of attacks following gastro-intestinal upsets are more than coincidental My impression was that the offending allergin was a food (Chapter 16) *However, in the form of therapy now described by the patient, the old* idea of auto-intoxication seems to be the guiding principle I could never generate much enthusiasm over the various methods of treatment that have risen to popularity since the *Bacillus bulgaricus* took the stage in spite of the fact that many ills are seemingly cured or avoided and longevity stands as a glowing reward at the end of the trail The one type of intestinal flora may be replaced by another acid producing type but it is a far cry from this fact to the proof that products of intestinal putrefaction are absorbed in sufficient quantities to affect the cardiac mechanism with the production of paroxysms of tachycardia

St Louis, Mo
April 15 1935

> I am still able to keep going but am definitely finished with all doctors My attacks after *all* the treatment *I have received in different* cities of the country are about the same as they were when I stopped in to see you in Philadelphia My heart continues its temperamental career It does its stunts at the most inconvenient times Last week I had a spell during an examination for life insurance and the company would not issue a $10 000 increase I have spent a sizable sum on doctors during the past year and if all the electrocardiograms I have had taken were collected and placed end to end they would form a cardiac race course reaching from here to Philadelphia I am going to be my own doctor for a while for I certainly cannot be much worse than I am now

A discouraged patient! However it is not entirely the fault of the physicians he has seen for he has not stayed in one place long enough for a thorough study to be made The therapy has been mainly for the seizures and the patient s manner of living in itself plays no small part in producing these frequent recurrences

Cincinnati Ohio
June 19 1936

> No doubt you have forgotten all about me by this time but I think that you ought to know how I finally obtained relief from my attacks I did not take any medicine or see any doctors for six months after I last wrote to you I had to continue at work but the attacks came on so often that I was quite miserable most of the time and lost considerable weight Last October while I was motoring through a small town in Ohio I decided to apply for medical aid once more This time instead of choosing a specialist who would have taken another dozen *feet of film of my*

> heart beat and have gazed at me through a fluoroscope I walked into the office of a general practitioner I told my story again and the old man was able to see me in one of my spells He then reached in the drawer of his desk and from among other things pulled out a handful of digitalis pills (that you had always told *me I did not need) and advised me to take one after each meal* for five days and then one every day He told me to take a two weeks vacation and return at the end of that time to see him I followed his instructions to the letter chiefly because he did not order a couple of dozen laboratory tests and puncture me with a hypodermic needle or try to force an entrance into some region of my body with a pipe line During those two weeks I did not have a single attack When I saw him again he told me to take one of the pills every day and go back to work I have not had a spell for eight months and I am sure that I am cured

Many times I have advised my surgical friends not to administer digitalis when their patients emerging from the anesthetic happen to have one of these attacks of paroxysmal tachycardia to which they may have been subject for years I try to demonstrate the quiet breathing the lack of any sign of congestive failure the dry lung and the normal temperature Even the serene countenance of the patient fails to convince the worried surgeon and when I return to the ward the next day I generally note that digitalis has been continued until the abrupt cessation of the abnormal rhythm Post hoc ergo propter hoc is a belief not entirely confined to lay circles However I still preach the doctrine that digitalis is poor therapy for this group of patients who have paroxysms of tachycardia when they have otherwise normal hearts A letter like this one forces me to admit the exception In a small group when all other measures fail complete digitalization with the continuance of maintenance dosage may bring relief The country doctor tried this and succeeded He was most up to-date in his method of using digitalis and in establishing proper maintenance allowance over a long period He was also able during the course of one visit to gain the patient s confidence and insist on a vacation The rest played no small part in the cure

Paroxysmal tachycardia is rarely met in children Tarran and Jennings[37] report 52 cases in literature from 1892 to 1935 in patients under 15 In a patient recently reported by Wright[43] 17 paroxysms were observed in a child of six years who had an otherwise normal heart Many of these were immediately terminated by 5 mg doses of mecholyl administered hypodermically There was a strong emotional factor in this Jewish child inasmuch as the paroxysms did not occur while she was in a convalescent hospital but immediately reappeared upon her return to the environment of her home I recently observed a paroxysm of auricular tachycardia in a Jewish child of five that lasted two weeks and resisted all forms of therapy that have been described Studies made during and after the

seizure showed a normal heart Food allergy was the background suspected in this case

### Paroxysmal Ventricular Tachycardia Complicating Acute Coronary Occlusion

**Case 72** F C an unemployed accountant of 56 was well except for the presence of elevated blood pressure for some years until an hour before admission to the hospital At this time following a heavy meal he had a sudden attack of severe precordial pain radiating to both sides of the neck It was promptly followed by vomiting and collapse When seen in the receiving ward the patient was in shock with a pulse so rapid that it was impossible to count the rate accurately Death occurred while the tracing shown in Fig 245 was being taken

Clinical Diagnosis A Etiologic Hypertension B Anatomic Cardiac enlargement Acute coronary occlusion C Physiologic Paroxysmal ventricular tachycardia D Functional Classification Class 4

Discussion Paroxysmal ventricular tachycardia is a much more serious arrhythmia and generally occurs in the presence of grave heart disease It is not infrequently associated with coronary accidents similar to the one described above Slight irregularities in the rhythm may serve to make the diagnosis at the bedside and differentiate from paroxysmal auricular tachycardia Paroxysmal auricular tachycardia is characterized by its absolute regularity Careful auscultation in patients with ventricular tachycardia may also reveal alterations in the heart sounds that are important in the differential diagnosis In ventricular tachycardia the first heart sound will occasionally vary in intensity It may be louder with some beats and reduplicated in others due to the varying positions of auricular systole in the cardiac cycle

Vagal stimulation and the other measures suggested for paroxysmal auricular tachycardia have no effect in ventricular tachycardia Digitalis is valueless in fact it may even increase the rate in some cases The drug of choice in this emergency is quinidine It is effectual because the arrhythmia is in all likelihood caused by a circus movement in the ventricle This mechanism may be rapidly fatal unless treatment is prompt In these emergencies quinidine should be given intravenously (page 384) before the sudden burden of the arrhythmia on an already damaged myocardium terminates the picture

## AURICULAR FLUTTER

In auricular flutter the impulse for cardiac contraction arises from a wave that follows a regular path around the auricular musculature at a speed of 260 to 310 revolutions a minute The pulse rate in flutter depends upon the ability of the ventricles to respond to the rapid succession of stimuli it receives from this abnormal auricular wave At times this response is one to one but more commonly a ventricular contraction follows the stimulus of every second or third revolution of the circus movements in the auricle The onset of flutter is abrupt It may persist for a short while as a paroxysm or may continue unchecked for months or years

When flutter disappears it may be replaced by either fibrillation or normal rhythm

Flutter is a rare disorder encountered only 20 times in the first 3000 electrocardiograms taken at the Cardiac Clinic of the Woman's College Hospital Flutter may be observed in otherwise normal hearts or may complicate rheumatic arteriosclerotic or thyroid heart disease Occasionally *other toxic states of the myocardium may be responsible for its appearance*

The pathologist finds no characteristic auricular lesion in cases of flutter but this should not be surprising inasmuch as it is usually brought about by a reduction in the refractory period of the muscle which permits continuous passage of the original contraction wave The clinical symptoms produced by the sudden onset of auricular flutter vary Rarely there may be none at all and the condition may be brought to light at a routine examination In other cases the ventricular rate is too rapid to count particularly where a one to one response occurs In these cases the tax on the cardiac reserve is great and if myocardial disease is present signs of congestive failure may appear rapidly Unconsciousness from cerebral anemia in some cases has been reported Fortunately the ventricles do not respond to each stimulus but to every second or third revolution of *the flutter wave in the auricle in which event the pulse rate will be about* 150 beats per minute The response of the ventricle will occasionally vary every second third or fourth stimulus getting through the junctional tissues and *producing an irregular* pulse resembling fibrillation Usually however the pulse is rapid and regular When the attack is over the ventricular rate will fall suddenly to normal and any symptoms that may have been present will disappear quickly

A history of a rapid ventricular rate in a middle aged or elderly patient sudden in onset and present for some weeks suggests auricular flutter If carotid sinus pressure slows the ventricular rate the diagnosis can be made with certainty Exercise may speed up the ventricular rate in flutter and make the rhythm regular the opposite is true in fibrillation Flutter can be distinguished from a paroxysm of tachycardia on the basis of the *ventricular rate The simple paroxysmal tachycardias usually have higher* ventricular rates (180 to 230)

## ILLUSTRATIVE CASES

### PAROXYSMAL AURICULAR FLUTTER IN AN OTHERWISE NORMAL HEART

**Case 73** H T a male laborer of 46 was first seen January 10 1935 complaining of vertigo and precordial oppression accompanying the sudden onset of a rapid heart rate Except for the history of peptic ulcer the patient had been well until a month before the onset of the attack when he developed pains in the shoulders arms and back. Although vigorously treated by his physician with salicylates and baking he became worse and was unable to work On purely empirical grounds he was placed on sulfanilamide therapy After three doses of 1 Gm each he developed nausea slight cyanosis and sudden rapid cardiac rate On admission the pulse was 150 in all positions More rapid auricular pulsations were noted in the neck veins The heart size was not increased and the sounds

were of good quality. No murmurs were heard. The blood pressure was 100/80. Wassermann, blood sugar, complete blood count and blood urea were normal.

CLINICAL DIAGNOSIS A Etiologic Unknown (Toxic from sulfanilamide?) B Anatomic No cardiac enlargement C Physiologic Auricular flutter D Functional Classification Class I Therapeutic Classification Class C

**Discussion** On admission the tracing (Fig 143B) showed typical auricular flutter with a two to one ventricular response. The patient was in

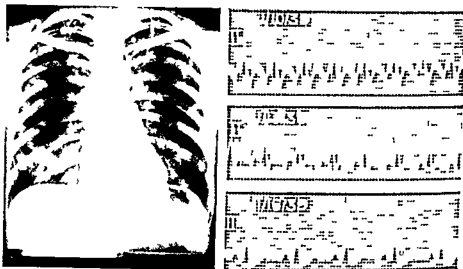



FIG 143 A Roentgenogram of chest The cardiac silhouette is normal in size and shape B The electrocardiogram Examination made on 10/1/39 shows presence of auricular flutter with a 2:1 ventricular response The next strip from the same lead three days later following the administration of 0.9 gram (13½ grains) whole leaf of digitalis Three days later (10/16/39) after 1.8 grams (27 grains) of digitalis whole leaf had been given the drug was discontinued Normal rhythm is now present Note depression of the S T intervals

good condition in spite of the continuation of the rapid ventricular rate, consequently it was decided to digitalize him slowly. The next tracing was taken three days later after nine tablets each containing 100 mg (1½ grains) of whole leaf of digitalis had been given. When a total of 18 tablets had been given the digitalis was stopped, and normal rhythm appeared spontaneously.

Administration of digitalis usually abolishes auricular flutter by converting it into auricular fibrillation. In this patient we see a return to normal rhythm without the intervening fibrillation. However there may have been a very short period of fibrillation following the disappearance of the flutter that was not observed. Since large doses of digitalis are needed to produce an effect in the presence of auricular flutter, the patient should be kept under constant observation while the drug is being given. Warnings such as anorexia and a slight nausea may be overlooked, but the ap

pearance of frequent premature beats in the tracing should always be considered a signal of the approach of dangerous toxic rhythms The digitalis should then be stopped Normal rhythm usually returns If there is no restoration of sinus rhythm in one week in patients who show no signs of mitral disease or auricular enlargement quinidine may be considered The patient now under discussion would have been an excellent case for quinidine therapy if normal rhythm had not returned following digitalization Likewise if forced to abandon the use of digitalis because of the appearance of toxic symptoms quinidine may be begun in a few days After the usual preliminary test dose of 0 2 Gm (3 grains) a 0 3 Gm (5 grains) capsule is given every four hours (four times daily) If this does not restore normal rhythm in three days it can be given five times daily If there is still no effect the dose can be increased every two days until a total of 2 6 Gm (40 grains) a day is reached In extreme emergencies where the abnormal rhythm is threatening life this amount may be exceeded in an attempt to restore sinus rhythm and save the myocardium In less urgent cases it is not wise to exceed 2 0 Gm to 2 6 Gm (30 to 40 grains) of quinidine daily Where the paroxysm of flutter is successfully abolished by the use of quinidine it is essential to continue the drug in maintenance dosage of 0 3 Gm (5 grains) three times daily In patients who have mitral disease and a large left auricle, it is a wiser course to accept the fibrillation and efficiently control the ventricular rate by digitalis

With the exception of a report of a transient nodal rhythm by Dozzi[81] following an initial dose of 5 4 Gm (80 grains) of sulfanilamide I am not aware of any reports in the literature of the appearance of toxic rhythms following this commonly used drug Considering the amount of the drug that must be consumed by all types of ambulatory and hospitalized patients if cardiac manifestations are common we would have seen more instances during the past years This patient and the patient of Case 77 are the only ones that I have encountered where the relationship between the onset of the arrhythmia and the exhibition of sulfanilamide suggested the possibility of toxic action In both cases the appearance of a paroxysm closely followed ingestion of the drug and in each instance the paroxysm was the only sign of heart disease encountered after complete studies were made Certainly fear of any cardiac complication should not deter us in the rational use of sulfanilamide or its derivatives

### Auricular Flutter Accompanying Rheumatic Heart Disease

**Case 74** Mrs E G a housewife of 29 when first seen was complaining of palpitation and rapid heart action She gave a history of two attacks of rheumatic fever Examination showed a pulse of 150 B P 110/74 The orthodiagram suggested the presence of mitral stenosis and regurgitation although the physical signs were not conclusive in the presence of such a rapid cardiac rate The electrocardiogram showed auricular flutter (see Fig 28)

Clinical Diagnosis A Etiologic Rheumatic (Inactive) B Anatomic Cardiac hypertrophy Mitral stenosis Mitral regurgitation C Physiologic Auricular flutter Functional Classification Class 1 Therapeutic Classification Class C

**Discussion** When this patient was first examined her ventricular rate was 150 There was no decrease in her exercise tolerance the lung fields were clear and her color was excellent She was given a tablet of the whole leaf of digitalis 0 1 Gm (1½ grains) after each meal for one week (weight 140) and was allowed to be out of bed but not out of the house during this time At the end of one week the pulse was slower and totally irregular An electrocardiogram (see Fig 228B) showed that fibrillation had replaced the flutter consequently the digitalis was entirely withdrawn and the patient instructed to return in another week At the third visit normal rhythm was present (see Fig 228C) At least half of the cases of auricular flutter when similarly treated will show a return to normal rhythm in this classical fashion

If advanced mitral stenosis is present and normal rhythm does not appear it is far better to continue the digitalis in daily maintenance dosage particularly if the ventricular rate is well controlled rather than attempt to restore normal rhythm by the use of quinidine If successful and sinus rhythm returns it soon gives way again to flutter or fibrillation so there is less risk if the ventricular rate of fibrillation is reduced and maintained at 70 beats per minute by digitalis

When this patient was examined a year later flutter had returned (Fig 228D) This time when fibrillation was produced, the digitalis was continued in maintenance dosage The rest of this patient s treatment was governed by subsequent developments in the course of her rheumatic heart disease (Chapter 3)

## AURICULAR FIBRILLATION

The most common cause of a perpetual arrhythmia is auricular fibrillation When viewed in the laboratory animal the fibrillating auricles show no co-ordinated systole twitchings and undulatory movements suggest incessant activity of the entire musculature produced by the irregular course of the fibrillation wave In flutter (see Fig 225) the pathway of the circus movement is the same at each revolution In fibrillation (see Fig 229) the course varies and impulses arrive at the A-V node at irregular intervals This accounts for the total irregularity of the rhythm in fibrillation

Auricular fibrillation in young people generally complicates the later course of mitral stenosis As a rule care should be used in making the diagnosis of fibrillation in patients less than 15 years of age although at times this arrhythmia may complicate congenital lesions (page 550) In later life auricular fibrillation frequently accompanies arteriosclerotic or hypertensive cardiovascular disease Rarely is it associated with aortic regurgitation and for this reason is seldom met in syphilitic heart disease

Recognition of auricular fibrillation usually presents little difficulty If the rhythm is irregular and the rate exceeds 120 per minute this arrhythmia is almost certain to be present If digitalis has slowed the ventricular rate

to 60 or below the diagnosis may be more difficult However it is well to remember that exercise increases the heart rate and accentuates the irregularity when auricular fibrillation is present

## ILLUSTRATIVE CASES

### Rheumatic Heart Disease with Auricular Fibrillation and Congestive Failure

**Case 75** V P a white American janitor of 4 had a single attack of rheumatic fever in 1928 at th age of 30 He was well until the summer of 1938 when he noticed increasing dyspnea on stairs This became worse until three months later edema of the feet appeared at night When first seen in February 1939 there was orthopnea and anasarca and the pulse was totally irregular with a precordial rate of 150 The heart was ncreased in size in all diameters and there was a systolic and a diastolic murmur at the cardiac apex The pulmonic second sound as accentuated

Clinical Diagnosis A Etiologic Rheumatic Inactive B Anatomic Cardiac hypertrophy Mitral stenosis Mitral insufficiency C Physiologic Auricular fibrillation Congestive cardiac failure D Functional Classification Class 4 Therapeutic Classification Class E

**Discussion** In this patient the onset of congestive failure was attended by a change from sinus rhythm to auricular fibrillation The ventricular rate was rapid and consequently the stage was set for a good therapeutic result In patients who have cardiac failure and rapid auricular fibrillation a great deal may be expected from the prompt use of digitalis in full dosage The bombardment of the responsive ventricle by the impulses from the fibrillating auricle is lessened many of the inefficient feeble beats are eliminated the pulse deficit disappears diuresis begins and the signs of cardiac failure recede Subjective improvement parallels the changes produced by this drug and the patient is pleased mightily

Examination of this patient five days after the administration of 1 3 Gm (20 grains) of digitalis whole leaf showed continued fibrillation but a much slower ventricular rate No attempt was made to restore normal rhythm because of the extent and type of the lesion When the ventricular rate reached 70 the digitalis was cut to 0 1 Gm (1½ grains) of the whole leaf daily This maintenance dose will be necessary for the rest of the patient s life One injection of mercupurin 2 0 cc was given at the start of the treatment to help the digitalis clear the edema The same result would have been achieved eventually without the mercupurin in this patient

### Paroxysmal Auricular Fibrillation—No Other Evidence of Heart Disease

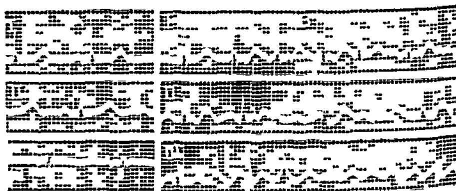
**Case 76** Mrs A C W an American house ife of 61 was first seen n 19 9 with the chief complaint of attacks of rapid irregular heart act on These had been experienced on the a erage of three times a year for the past 14 years

Physical Examination BP 1 8/80 The heart was normal in size and shape (Fig 144A) There were no m rmurs Other features of the exam nat on were irrelevant except for the presence of a small calc fied fibroid tumor At the time of the next seizure an electrocard og am was obtained (F 144B) which showed the p esenc of aur cula

fibrillation Normal rhythm returned spontaneously one hour later (Fig 144B) From 1939 until 1940 many attacks similar to this one have been observed There are no signs *of congestive failure during the attacks The heart has not increased in size* as shown by frequent orthodiagraphic studies The basal metabolic rate has been taken many times, the figures ranging from minus eight to plus four



A



B

FIG 144 A Roentgenogram The heart is not enlarged B The electrocardiogram (a) normal rhythm (b) taken during a paroxysm Auricular fibrillation is present

DISCUSSION The occurrence of paroxysmal auricular fibrillation in *patients exhibiting no other signs of cardiac disease is relatively rare* In a study of 200 cases of paroxysmal auricular fibrillation Parkinson and Campbell[393] found that 9 per cent showed no apparent cause for the occurrence of this marked arrhythmia White and Jones[393] in an analysis

of 376 cases of auricular fibrillation found that 8 0 per cent were free from heart disease

In the five patients that I have studied the inciting factors in precipitating the paroxysm of fibrillation were alcohol in two a gastro-intestinal upset in two and unusual exertion in one In the patient I have selected for discussion here the attacks have been present for 25 years and always follow a digestive upset

Since there are no gross or microscopic lesions of the auricular musculature characteristic of fibrillation we may assume that the presence of the arrhythmia does not depend upon a definite structural defect in the heart It is primarily a functional alteration and may be produced in many instances by extracardiac neurogenic forces

Hyperthyroidism is the first thought when no explanation for the paroxysms of fibrillation is evident at the time of the initial study Many cases will ultimately fall into this group particularly if the fact is kept in mind that thyrotoxic heart disease may exist in the presence of a normal basal metabolic rate A complete study should be made of the skin the eyes the neck the weight changes and the hands for the presence of tremor before deciding against the thyroid as the dominating influence The physical signs should be weighed with the laboratory evidence

When paroxysmal auricular fibrillation is present the heart should be carefully watched between attacks Evidence of mitral stenosis should be sought in the character of the first heart sound and the presence of early diastolic murmurs and the size and shape of the heart on fluoroscopic examination A large auricle in one of the oblique positions on fluoroscopy may point to an overlooked mitral lesion

All of the patients that I have studied who have suffered from paroxysms of auricular fibrillation with no other evidence of heart disease have had one thing in common This was a marked nervous instability All were emotional and showed a tendency to over reaction to the ordinary stimuli of life In each instance I suspected that the trigger mechanism was the thyroid gland but could not prove this view to be correct It is certainly true that this type of person presents much more opportunity for the occurrence of abnormal stimuli that are reflected in the cardiac mechanism by the sudden onset of paroxysms of auricular fibrillation How the irregular circus movement in the auricle is started in these cases remains unknown It must be closely related to the mechanism operative in disturbances of the thyroid gland The trigger may be the adrenal

In the patient under discussion the investigation was first directed toward the thyroid status Since repeated determinations of the basal metabolic rate showed no elevation and a therapeutic trial of iodides was entirely ineffectual in lessening the frequency of the seizures studies were carried further and an allergic cause was sought

While I have seen allergy assume an important etiologic role in a few cases of paroxysmal auricular tachycardia I have never met it as the exciting factor in paroxysmal auricular fibrillation However this patient

was completely studied by Dr Kern The result of his investigation and a discussion of the case from the allergic standpoint will be found on page 459

Quinidine in 0 3 Gm (5 grains) doses was found to be invariably successful in restoring normal rhythm in this patient Consequently when attacks appeared with increasing frequency she was placed on maintenance dosage of the drug as a prophylactic measure A 0 3 Gm (5 grains) capsule was given twice daily and later this was increased to three times daily While occasional small doses of quinidine were very well tolerated when maintenance doses were begun minor symptoms were complained of at the end of the second week These consisted of headache vertigo nausea and finally tinnitus When the maintenance dosage was decreased paroxysms returned and larger doses were found to be required to restore normal rhythm The patient finally requested that she be allowed to take the quinidine at the time of the paroxysms and stop the daily ration of the drug She stated that she would rather run the risk of an attack at an inconvenient time than tolerate the annoying symptoms that accompanied maintenance doses of quinidine

## Congestive Cardiac Failure Induced by a Paroxysm of Auricular Fibrillation in a Senile Heart

**Case 77** W M a male clerk of 70 when first seen was complaining of dysuria frequency and nocturia of three days duration The temperature was 101 F pulse 90 and regular and the heart was normal in size and shape There were no murmurs The urine showed a light cloud of albumin and was loaded with pus and blood cell When an unidentified streptococcus was cultured from the urine a diagnosis of urinary tract infection was made and the patient was given 0 Gm (30 grains) of sufanilamide as an initial dose and 1 0 Gm (15 grains) every four hours When examined the next day the pulse was 140 and totally irregular Orthopnea and cyanosis were present Rales were heard at the lung bases

**Discussion** Paroxysms of auricular fibrillation not uncommonly follow toxic states for example those produced by infectious diseases like pneumonia or the ingestion of a drug or poison in large quantities In this old gentleman it was difficult to decide whether to associate the onset of auricular fibrillation with the toxemia of the urinary tract infection or the sulfanilamide

The therapy employed was based on the signs of congestive failure that appeared so quickly dyspnea cyanosis and finally pulmonary edema The patient had not previously been taking digitalis consequently an initial dose of strophanthin 0 4 mg (1/150 grain) was given intravenously and in addition a hypodermic injection of 15 mg (¼ grain) of morphine sulfate There was marked improvement in the congestive signs in two hours At this time tablets of digitalis whole leaf were started by mouth In 24 hours normal rhythm returned

In Case 76 the paroxysms of auricular fibrillation caused complaints of palpitation and vertigo but no signs have ever appeared that point to the slightest circulatory insufficiency Consequently when we see how well

the heart muscle has withstood these repeated assaults for many years it is small wonder that we speak well of its functional capacity and doubt the presence of cardiac disease

In Case 77 however the situation is different In this old man the sudden burden of the arrhythmia overtaxed the myocardial capacity and precipitated signs of failure The intravenous administration of strophanthin was called for in such an emergency and it was followed by rapid improvement Digitalization was completed using the whole leaf tablet by mouth and maintenance dosage was then continued

## HEART BLOCK

This arrhythmia was recognized and described clinically before the specialized tissue of the conduction system was discovered The work of many investigators during the last part of the nineteenth century proved that impulses are conducted from the auricle to the ventricle over the A V or His bundle If the tissue of the normal bundle is clamped lightly in the experimental animal the function is interfered with and the length of time for an impulse to pass from auricle to ventricle is increased If the clamp is tightened the time is still further lengthened until an occasional beat is dropped Further compression will cause higher degrees of block until the process is complete When this occurs the auricles continue to beat at their usual rate while after a pause the ventricles respond to a new (or idioventricular) center just below the level of the lesion and resume their contractions at a much slower rate During the time of ventricular adjustment cerebral anemia usually occurs If the pause is longer it may be attended by coma and convulsions A similar sequence of events has been observed clinically when conduction through the bundle of His has been seriously affected by a disease process The attacks of cerebral anemia may cause vertigo and faintness or may be attended by coma and convulsions These attacks have been termed Adams Stokes seizures although Adams and Stokes were by no means the first to describe them

Since the electrocardiograph records faithfully the time consumed by the passage of the contraction impulse from auricle to ventricle slight delays are readily detected by this method (page 615) The presence of even a mild degree of inflammatory change in the neighborhood of the bundle or interference with a portion of the coronary blood supply may be reflected at once in the prolongation of the P R interval of the electrocardiogram Many times this is the only sign present to suggest cardiac involvement during the course of acute rheumatism or diphtheria The prolonged P R intervals may be missed since few patients are studied by the electrocardiographic method However when the heart block progresses to the stage of dropped beats or to complete dissociation it will attract clinical attention if the pulse is carefully studied

The anatomic change present in infectious states may be a temporary one and complete functional recovery of the conduction system may be

possible following resolution of the inflammatory exudate The electrocardiogram will then return to normal Temporary change in the conduction time may also be associated with excess vagal stimulation, asphyxia uremia or it may follow the toxic action of certain drugs like digitalis or quinidine Coronary disease particularly occlusion may cause a more permanent alteration to occur although even here collateral circulation may *make possible the return of normal function in a few days (see Fig 243)* Infiltration of the conduction tissues by a secondary tumor growth may produce heart block of a more permanent nature because of destruction of the tissue (page 407) Heart block rarely results from congenital deformities in the septum (page 543)

The gumma of syphilis as a cause of complete heart block is most infrequent although this is generally the first one mentioned by the student Invasion of the bundle from the vegetative growths of subacute bacterial endocarditis is likewise unusual Graybiel and White[141] in a recent survey of 72 cases of complete A V dissociation found the cause *to be coronary disease in 47 congenital heart disease in 4 possible con*genital heart disease in 2 rheumatic heart disease in 5 syphilis in 3 diphtheria in 4 while the remaining 9 cases were of mixed or uncertain etiology

At postmortem when sections of the heart are made and the conduction system is inspected the degree of change by no means parallels the clinical symptoms For example only a thin strand of tissue may be found remaining yet during life the conduction system may have shown perfect function In other cases a great deal of apparently good tissue may be seen in hearts of patients who showed complete block during life The *only explanation in the latter instance seems to be the chemical changes* present during life in and about the bundle tissue caused by anoxemia and circulatory stasis In cases where no change at all is seen in the bundle tissue and complete block was known to have been present we must consider vagal action and the effect of certain drugs

While the electrocardiogram may show a prolongation of the P R interval as the only evidence of an acute myocarditis two physical signs that will aid in establishing the diagnosis may be detected by the careful clinician If the time interval between the auricular and ventricular systole is lengthened a splitting of the first heart sound may occur The first element of this sound is caused by auricular systole Again if a mitral stenosis is present the characteristic rumbling murmur may change its position from presystole to early or mid-diastole for the same reason Where the degree of block is greater and occasional dropped beats occur the pauses that accompany them may be detected in the radial pulse and the differential diagnosis from premature beats may be made by careful auscultation Close inspection may reveal a wave in the jugular veins produced by the blocked auricular contraction during the period of ventricular asystole

Auriculoventricular block is a symptom and not a disease Consequently in most of the following illustrative cases it will be noted that the treat

ment is that of the underlying condition causing the block. However, when the block is complete and causes a profound disturbance in the cardiac action with Adams Stokes seizures, it requires special treatment. In White's series of 72 cases symptoms related to the block itself occurred in 44 and in four instances were the probable cause of death.

## ILLUSTRATIVE CASES

### Prolongation of the P R Interval (First Stage Heart Block) During the Course of Acute Rheumatic Infection

**Case 78** C C, a male elevator operator of 23, was admitted to the Woman's College Hospital on May 7, 1936, complaining of backache and pains in the joints. The onset of the present illness was a week prior to admission, when a sore throat and evening temperature appeared. Physical examination on admission showed T 100, B P 116/76, pulse 88, rhythm regular, no cardiac enlargement and no murmurs. The joints showed no swelling or redness. An electrocardiogram showed prolongation of the P R intervals to 0 3 second.

Clinical Diagnosis A Etiologic Rheumatic Active B Anatomic No cardiac enlargement C Physiologic First stage heart block D Functional Classification Class 1 Therapeutic Classification Class E

**Discussion** The prolongation of the P R interval in this patient was a very valuable finding, suggesting at once the nature of the joint manifestations. An involvement of the heart by the rheumatic process was suspected and a diagnosis of acute myocarditis based on this finding. The treatment of the heart block in this instance is that of the underlying rheumatic process (Chapter 3).

### Complete Heart Block Complicated by Adams Stokes Seizures

**Case 79** Mr O F, an executive of 74, was first seen October 10, 1936, complaining of weakness, dyspnea and vertigo. Hypertension had been present for some years. Three months previous to the first examination marked edema of the feet appeared but cleared up on bed rest. The dyspnea persisted to the time of the first examination.

Physical Examination The blood pressure was found to be 180/110. Pulse 40. The heart was enlarged to the left on percussion, the left border measuring 1 5 cm from the mid sternal line and the right border 3 0 cm. An apical systolic bruit was heard, poorly transmitted in the direction of the axilla. The liver edge was palpable beneath the right costal margin. There was no edema.

Laboratory Data The first electrocardiogram (see Fig 213) taken 10/10/36 showed complete dissociation with auricular rate of 100 and ventricular rate of 40. Occasional ventricular complexes showed the presence of faulty intraventricular conduction.

An orthodiagram showed a heart of hypertensive shape with a cardiothoracic ratio of 0 51. It was possible to note the A V dissociation during fluoroscopic study.

Course The patient was examined again four months later (February 1937), at which time he still complained of weakness and dyspnea. In addition he stated that he had experienced two spells of sudden syncope, both following emotional upsets. Consciousness was lost on each occasion for less than one minute. There were no convulsive movements and recovery was prompt and complete.

An electrocardiogram taken on the second visit showed striking differences in the T waves in both direct and indirect leads. There had been no precordial pain or paroxysmal dyspnea; nevertheless these changes were ascribed to a coronary occlusion which had occurred since the last examination. The orthodiagram showed no essential

change The urine showed a trace of albumin fixation of the specific gravity (1 008) and both hyaline and light granular casts The blood Wassermann reaction was negative and the blood pressure reading was increased this time measuring 220/110

The next examination was mad 15 months later at the patient s home (May 20 1938) His interval history indicated a steady downhill course During the late winter and early spring months his spells of syncope had increased in frequency Th y were of longer duration and convulsive twitchings were reported to have taken place during all the seizures There was no incontinence of urine or feces Members of the family who witnessed attacks stat d that they were preceded by pallor However the onset of each attack was usually announced by the patient himself Cyanosis followed the pallor and the re pirations became frequent deep and noisy In a minute convulsive twitchings of the extremities appeared followed by return of consciousness We were able during the next 24 hours to witness many of these seizures They varied in length from less than a minute to over six minutes During the early shorter seizures the patient would recover and resume the conversation Electrocardiograms were continuously recorded The next day the attacks were longer in duration and consciousness returned more slowly Finally after an attack lasting six minutes consciousness was not regained During a terminal coma brief seizures continued until death nine and one half hours later Postmortem examination was not obtainable

Clinical Diagnosis A Etiologic Hypertension Arteriosclerosis B Anatomic Cardiac enlargement Coronary occlusion Relative mitral insufficiency C Physiologic Heart block with Adams Stokes seizures D Functional Classification Class 3 Therapeutic Classification Class E

Discussion The Adams Stokes attacks in this patient from the time of their onset 15 months before death appeared to have a direct relationship to emotional upsets During the last 48 hours of life these attacks varied in duration from one-half minute to six minutes becoming more prolonged and more frequent after the first 24 hours until the seizure that lasted over six minutes permanently eliminated consciousness Until the last 24 hours of life the patient was able to announce the beginning of every attack which always coincided with the disappearance of the radial pulse Pallor followed and the respirations became deep and noisy There were no convulsive movements noted at this time although the muscles about the neck and face seemed to be tighter The pallor continued changing in less than a minute to cyanosis When the pulse beats were felt the patient s face became purplish red and convulsive movements occurred Apnea followed the color change in the face

The series of events observed in this patient during successive Adams Stokes attacks is not fortuitous but dependent on a definite relationship between respiration and circulation that Formijne[103] has observed in a series of clinical and experimental studies With the onset of the attack all blood flow ceases Respirations continue giving the blood stagnant in the lungs a chance to become more completely saturated with oxygen and to lose a great deal more of its carbon dioxide than ordinarily occurs With recovery the first substantial cardiac contraction sends out this pooled hyperventilated blood Apnea results when it strikes the respiratory center The patient s color undergoes a marked change with the arrival of blood rich in oxygen in the capillaries of the face The convulsive movements that follow at this point arise from the alkaline state of the blood

since the hyperventilation received in the lungs during the cessation of circulations washed out an excess of carbon dioxide

A study of this patient s electrocardiograms before the seizures suggested a coronary accident as the cause of the complete block The attacks were preceded by the appearance in the tracing of occasional ventricular extra systoles which became more frequent and then appeared in short runs of three or more leading into the attack A very rapid ventricular rhythm was seen during some of the periods of unconsciousness During others stand still of the ventricles was observed

### Treatment

The proper management of these attacks depends upon the electrocardio graphic findings Where ventricular standstill causes the cerebral anemia and syncope the treatment consists of the intramuscular injection of ½ to 1 cc of a solution of epinephrine hydrochloride U S P between attacks to stimulate the idioventricular center While this drug is useful in pre venting seizures it should be administered with great care Some observ ers[114] have successfully combined epinephrine with barium chloride The latter drug increases the irritability of the area in the ventricle below the level of the block and makes it more susceptible to the action of the epinephrine In the presence of complete standstill of the ventricles the epinephrine should be given by intracardiac injection[30 334] inasmuch as action of the drug by any other route is unlikely during the period of cardiac standstill Epinephrine tends to increase both auricular and ven tricular rates in these instances

While a life saving procedure in the presence of standstill epinephrine may be actually harmful if the prefibrillary type of ventricular tachycardia or ventricular fibrillation are present (see Fig 214) These abnormal rhythms are evidence enough of the irritability of the tissues An accentua tion of this state by the introduction of epinephrine is contraindicated since it has been shown[1 3 335] to produce or prolong ventricular fibrilla tion which is likely to result in death

The use of ephedrine in complete heart block was first reported by Miller [71] His patient had complete A V dissociation but no Adams Stokes seizures and showed increase in auricular and ventricular rate and a change in the shape of the P waves and ventricular complexes following hypo dermic injection of 100 mg (1½ grains) Stecher[3 3] reported favorably on ephedrine when used in a similar case having Adams Stokes seizures fol lowing ventricular standstill The drug was given by mouth in 30 mg (½ grain) doses three times daily for one week and then 20 mg (1/3 grain) three times daily for two weeks During this time there was complete relief from attacks Cheer Tung and Bien[55] found that patients with complete heart block responded to ephedrine quite differently and suggested the administration of atropine to prevent the reflex stimulation of the vagus and the rise in blood pressure following ephedrine The combination of these two drugs does not abolish the complete block

Wedd recently reported a case of complete heart block resulting from rheumatic infection in a woman 41 years old Several Adams Stokes seizures were observed and epinephrine was without effect Following the injection of 2 mg (1/30 grain) of atropine sulfate deep into the deltoid muscle, the heart began to beat normally no further syncopal attacks occurred and the patient made an uneventful recovery This observation is of great therapeutic interest and points to the action of the vagus in cases of heart block following rheumatic fever It agrees with the studies of Gross and Field who found minimal changes in the conduction system in rheumatic fever and concluded that vascular changes were more important than exudative Vagal release in these cases may increase the coronary flow

Poole and Wilkinson[303] have recently reported a case of complete heart block in a man of 72 where reversion to a normal rhythm occurred after administration of small doses of benzedrine sulfate (amphetamine sulfate) Twelve hours after administration of the first dose of 10 mg (1/6 grain) by mouth the pulse rose to 68 and there was improvement in the clinical status of the patient When the drug was withheld the block returned and it was again given with identical results The dosage of amphetamine was therefore maintained These authors believe that the drug is superior to epinephrine and ephedrine for this purpose Amphetamine is closely related chemically to both ephedrine and epinephrine and possesses similar pharmacologic properties, so this action in heart block is not unexpected

The treatment carried out in the patient under discussion was as follows When first seen a capsule containing theophylline ethylene diamine 0 12 Gm (2 grains) and phenobarbital 15 mg (¼ grain) was given after meals When evidence of congestive failure appeared, he was completely digitalized and then maintained on 0 1 Gm (1½ grains) of the whole leaf daily When the Adams Stokes attacks appeared the patient was given ephedrine hydrochloride in 20 mg (1/3 grain) doses every four hours by mouth Later a hypodermic injection of 30 mg (½ grain) was given every two hours We were afraid of epinephrine injections because of the nature of the arrhythmia seen in the electrocardiograms during the seizures

## Hypertensive Cardiovascular Disease Complicated by Complete Heart Block and Adams Stokes Seizures

**Case 80** Miss A M a retired school teacher of 76 was first seen on October 7 1938 following a spell of unconsciousness The patient had been in fair health until a week before when she suddenly became dizzy and lost consciousness During the seizure there were convulsive movements A similar attack occurred the day before admission to the hospital It was followed by vomiting and some sense of fullness in the chest

Physical Examination B P 168/78 Pulse 40 The heart was enlarged to percussion in all diameters the left border reaching 13 cm to the left of the mid sternal line The lungs were clear and the liver border was palpated two fingers breadth below the costal margin All reflexes were normal No edema was noted

Laboratory Data The blood Wassermann reaction was negative Blood count hemoglobin 7? per cent (Sahli); R B C 3 650 000; W B C 8 ?00 Differential neutrophiles 64 per cent lymphocytes 36 per cent The urine showed specific gravity of 1 010 a heavy trace of albumin no sugar and a few hyaline casts Blood urea nitrogen

18 mg The roentgenogram of the chest showed the heart to be of the hypertensive shape with widening in all diameters

COURSE On the first day of a two weeks stay at the Woman's College Hospital this patient had a typical Adams Stokes seizure She gave warning of its approach during the taking of an electrocardiogram consequently the whole seizure was recorded (see Figs 15 and 216)

DISCUSSION Following the Adams Stokes seizure the patient was placed on barium chloride in 60 mg (1 grain) doses after meals There were no other attacks during her stay in the hospital Six months later a follow up note from her physician states that the medication had been continued with no recurrence of the seizures I do not believe however that her freedom from syncopal attacks came as a direct result of the therapy since there is always a tendency for these attacks to cease spontaneously They occur more frequently in some patients than in others for example in Case 79 the seizures were so frequent that they were not all recorded Usually the remedy that is administered at the time of the spontaneous recovery gains an undeserved reputation that it loses in a few years No specific drug for Adams Stokes seizures has yet been found and a multiplicity of remedies makes the therapy of this rare disease appear to the casual observer to be in a confused and unsettled state

Early experimental work showed that the salts of barium and calcium increased the irritability of cardiac muscle and in 1923 barium chloride was first used clinically Good reports appeared on all sides and its action combined with adrenalin caused favorable comment Starting with the report of Parsonnet and Hyman [94] who used the drug unsuccessfully in eight cases of complete heart block with Adams Stokes seizures the tide has recently turned against barium chloride

Lueth [40] has advised the use of metrazol in complete heart block with the Adams Stokes syndrome In four of his cases two were greatly benefited while in the other two it proved to be of little value However the drug has no untoward effects even when used over long periods a fact which recommends it when other measures fail Metrazol (cardiazol) is pentamethylene tetrazol a substance with camphor like action is soluble in water withstands heat and therefore can be safely and easily sterilized for subcutaneous injection The hypodermic injection varies with the patient Usually it is wise to start with small doses (½ to 1 cc of a 10 per cent solution) subcutaneously and at the same time to administer the drug by mouth Larger doses (5 to 7 cc of a 10 per cent solution) have recently been given intravenously in schizophrenia with few permanent effects on the heart In the Adams Stokes cases the beneficial action of the drug comes about through its stimulation of the vasomotor tone and respiration The same action recommends its use in cases of circulatory collapse

Thyroid U S P has been recommended for the prevention of Adams Stokes seizures in doses of ½ to 3 grains daily to increase the irritability and rate of the ventricles

It must be emphasized that complete heart block and Adams Stokes

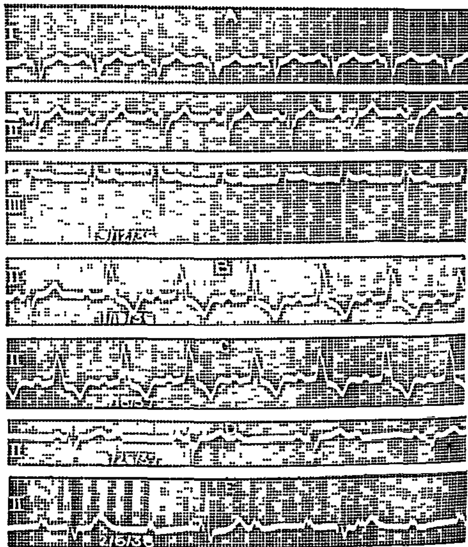


FIG 145 A series of electrocardiograms of a white male of 66 suffering from hypertensive cardiovascular disease and angina B P 10/100 heart moderately enlarged when first seen On careful regulation of regime the clinical status showed *no change* during the next three years The progress of his lesion is reflected in h electrocardiograms A Three standard lead taken at the time of his first examination Note marked left axis deviation and QRS B Lead _ from a tracing made two months later Note the transition from normal beat to bundle branch block There is also a slight prolongation of the P R Intervals No digitalis had been given C Two months later the bundle branch block persists D Seven months later A _ 1 heart block is present The bundle branch lesion is no longer in evidence E Six months later The heart block is now complete Tracings similar to this one were obtained over the course of the next two years The patient died in February 1940 six months after the onset of congestive cardiac failure No Adams-Stokes seizures appeared at any time

syndrome are not synonymous Heart block may be present for many years without the occurrence of faintness syncope or convulsive seizures This is well illustrated by the patient whose electrocardiogram appears in Fig 145

### Complete Heart Block Caused by Tumor Metastasis—Autopsy

**Case 81** C E F a white male laborer of 45 was admitted to the Philadelphia General Hospital complaining of swelling of the legs The onset was three years before admission when some edema appeared at night but the patient was able to work until ?/1/37 At this time he developed precordial pain increase in edema and cough

Physical examination showed B P 120/80 an emphysematous chest full of moist crepitant rales The liver was enlarged 3 cm below the costal margin There was no fluid in the abdomen The fingers showed slight clubbing and the ankles pitting edema moderate in degree The heart was enlarged to the left The apex beat was in the sixth interspace in the anterior axillary line and a soft systolic murmur was present over the apex No thrills Heart rate 60 to 70 and irregular

Laboratory Data Electrocardiogram showed right axis deviation and complete heart block The ventricular rate was more rapid than one would expect in heart block (60 to 90)

The roentgenogram showed cardiac enlargement and emphysematous lungs with diaphragmatic adhesions

Clinical Diagnosis A Etiologic Arteriosclerosis B Anatomic Cardiac enlargement C Physiologic Heart block Congestive failure D Functional Classification Class 3 Therapeutic Classification Class E

Course In spite of venesection digitalization and other measures directed toward the relief of the symptoms of cardiac failure the patient s course was rapidly downhill and he died two weeks after admission

Autopsy revealed about 200 cc of blood tinged fluid in the pericardial cavity The parietal pericardium showed no change but the visceral layer was covered with tumor nodules extending into the myocardium (Fig 146A) The left auricle and the right ventricle were filled with a mass of tumor tissue (Fig 146B) grayish red in color They were fairly firm not friable and were attached by pedicles to the region of the septum in places extending part way through the latter There was extensive tumor infiltration of the endocardium above the mitral ring but the valves were not involved in the neoplastic process The inferior vena cava was partially obstructed by large masses of tumor tissue in the right auricle The coronary arteries were unchanged

**Discussion** Metastatic tumor of the heart invading the septum and causing heart block is rare It must always be thought of however in patients with a primary tumor growth in any region of the body and circulatory symptoms of obscure etiology (Chapter 14) In this case the primary focus was thought to be a large ulcer in the stomach It was impossible to determine the exact type of tumor cell present either epithelial or lymphoid origin was suspected

## PULSUS ALTERNANS

### Hypertensive Cardiovascular Disease with Beginning Congestive Cardiac Failure—Pulsus Alternans

**Case 82** F H an Italian laborer of 64 was admitted to the Woman s College Hospital on 7/4 33 complaining of increasing dyspnea and edema He was examined in the cardiac clinic eight months prior to admission at which time the blood pressure was found to be 220/120




Fig 146 A Tumor nodules in epicardium B Tumor mass filling cavity of the right ventricle (Autopsy No 33 696 Philadelphia General Hospital)

PHYSICAL EXAMINATION The left cardiac border extended to the midaxillary line A systolic murmur was heard over the apex and there was dulness to the right scapular angle with the absence of tactile fremitus and breath sounds On admission the pulse rate was 1 0 with regular rhythm Half the pulse beats were found to come through at a blood pressure level of 200 at 190 the pulse rate suddenly doubled The diastolic level was 120 The weakness of the alternate beats was not appreciated on pulse palpation An electrocardiogram showed a left axis deviation and an inversion of T 1

CLINICAL DIAGNOSIS A Etiologic Hypertension B Anatomic Cardiac enlargement Relative mitral regurgitation C Physiologic Normal sinus rhythm Pulsus alternans D Functional Classification Class 4 Therapeutic Classification Class E

**Discussion** The detection of pulsus alternans in this patient confirmed the diagnosis of left ventricular failure and suggested a poor prognosis The treatment consisted of bed rest thoracentesis venesection and digitalization On this regime the patient improved and was edema free by the end of the first week in the hospital Two weeks after admission however he died suddenly during another seizure of paroxysmal nocturnal dyspnea or sudden left ventricular failure Characteristic alteration of the pulse appeared at intervals during the last two weeks of life

Pulsus alternans can be demonstrated best by a graphic tracing of the radial pulse However whenever its presence is suspected an attempt should be made to demonstrate it by the use of the sphygmomanometer To do this the cuff is inflated above the systolic level of the blood pressure As the mercury column drops slowly only one half of the pulse beats will be heard coming through As the mercury falls still further (range about 5 to 15 mm ) a level will be reached where the pulse rate is suddenly doubled In other words all the pulse beats will be heard at this second systolic level

Alternation has been attributed to the fact that the myocardium as a whole may fail to respond to each contraction impulse because of the presence of advanced myocardial disease The refractory fibers are scattered through the whole heart and are sufficiently numerous in certain disease states for their absence to be detected when the strength of the pulse beat is recorded graphically The difference at times may be appreciated by careful palpation of the radial pulse Pulsus alternans may accompany hypertensive cardiovascular disease when there is beginning heart failure or it may appear following an acute coronary occlusion Where very rapid cardiac rates accompany this phenomenon the prognostic significance is not the same for a healthy heart in paroxysmal tachycardia or flutter may be so overloaded that rest of some of the fibers may be a protection mechanism necessary for survival The prolongation of the refractory periods of some fibers causes alternation when seizures are prolonged However in these instances pulsus alternans disappears as soon as the paroxysm is over ALTERNATION IN THE HEIGHT OF THE QRS COMPLEXES OF THE ELECTROCARDIOGRAM IS NOT IDENTICAL WITH PULSUS ALTERNANS When mechanical alternation is not present in the pulse tracing or demonstrable in the mercury column of the sphygmomanometer the electrocardiographic alternation is of no clinical significance

# 13

# FUNCTIONAL HEART DISEASE

C'est l'imagination qui gouverne le genre humain NAPOLEON BONAPARTE (*Bourrienne Life* II, 2)

Many patients have 'heart disease' that is wholly in their imagination Considering the percentage of the modern population who possess the constitutional background for the development of a neurosis of some type it is small wonder that present day radio and newspaper agitation concerning the increase of heart disease turns attention in this direction Not infrequently the presence of a harmless systolic murmur discovered quite by accident or the misinterpretation of an electrocardiogram or roentgenogram by a physician is the starting point of years of invalidism Many times the sudden death of a near relative from cardiac disease focuses the attention of the patient on the heart Likewise a person of the neurotic type who learns of the presence of organic heart disease may at once develop symptoms out of proportion to the lesion The symptoms of a cardiac neurosis will then be superimposed on those of a definite circulatory disease

On the other hand symptoms of heart disease often are present in patients who are not victims of fear or of psychoneurotic states They are frequently produced in individuals who are subjected to excessive exertion and loss of sleep over long periods of time Among the Union forces during the Civil War this syndrome was first recognized and described by Da Costa as the irritable heart of soldiers During the World War (1914 1918), Sir Thomas Lewis gave the name effort syndrome to the condition and recently American writers have suggested the more appropriate designation neurocirculatory asthenia" The last term is to be preferred since it does not contain any reference to the heart

## NEUROCIRCULATORY ASTHENIA

Neurocirculatory asthenia is a readily recognized syndrome characterized by palpitation dyspnea easily produced exhaustion and at times by chest pain following slight exertion While common in soldiers it is not infrequently met in civilian practice It is most essential to distinguish this condition whenever possible, from the psychoneuroses presenting cardiovascular symptoms Some cases however may be encountered that show a combination of the effort syndrome and the cardiac symptoms of a psychoneurotic nature

When a nation mobilizes, men from all walks of life and from all but

the vital occupations are gathered together and subjected to the stress and strain of army life Forced marches drilling varying degrees of mental trauma and loss of sleep are daily experiences If these are long continued circulatory symptoms develop sooner in some than in others Normally following exertion any untrained person shows breathlessness rapid heart action palpitation vertigo and faintness even precordial pain may accompany extreme effort Exhaustion and tremor often appear when activity ceases and if the oxygen debt is great breathlessness continues These same sensations occur in men subjected to army routine and cannot at the start be considered abnormal However as time goes on these symptoms are produced by less than ordinary amounts of exertion Consequently while the symptoms are not abnormal they are so easily produced we say the patient suffers from 'effort syndrome or neurocirculatory asthenia

Lewis found that the group invalided home from the British expeditionary forces in 1915 because of this disability was a mixed one [9] In it were included soldiers who showed no signs of actual heart disease but evidences of constitutional inferiority Many were of the hyposthenic type with long flat chests and family histories of psychoneurosis epilepsy or insanity Others were from divisions at the front line where activity had been great and the sojourn long Consequently exhaustion loss of sleep and continued strain were the precipitating factors In another group, the symptoms of neurocirculatory asthenia came on during convalescence from illnesses like tonsillitis influenza or pneumonia Others showed previously unrecognized incipient tuberculosis or other infections while a few showed beginning heart involvement All had the same symptoms but a wide range of etiologic factors Consequently the condition became very difficult to analyze in a truly scientific manner In the army treatment had to be prescribed for these patients as a class while in civil life individual and accordingly more successful management is possible

## Symptoms and Signs

**The breathlessness or dyspnea** of neurocirculatory asthenia is not present when the patient rests but appears very quickly when slight exertion is attempted It is probably of nervous origin since the vital capacity of this group is only a little below normal Excessive fatigue and exhaustion generally come on very quickly after slight exertion and are accompanied by tremor in many cases These symptoms closely resemble those produced by hypoglycemia following violent exercise Likewise pain over the region of the heart and even hyperesthesia of the adjacent skin surfaces occur on slight exertion The chest pain is an important symptom and must be differentiated from the pain of angina

**Palpitation Dyspnea and Fainting** Palpitation commonly attends slight exertion in effort syndrome and is generally caused by sinus tachycardia Arrhythmias are rare but extrasystoles occasionally are present Fainting occurs in this group of cases generally following slight trauma like the taking of blood from an arm vein It is usually vasovagal in origin

Examination of the heart shows little evidence of disease The only abnormalities will be the tachycardia and the increased forcefulness of the heart beat The cardiac rate is not uncommonly 85 per minute at rest, while higher rates are observed in patients who are ambulatory After exercise the pulse rates mount quickly in these cases and return very slowly to normal The blood pressure varies It is low in many patients at rest but tends to show an exaggerated response to exercise

INCIDENCE

Neurocirculatory asthenia is not uncommon in civilian practice The stress and strain of life overwork exhaustion and worry bring on the syndrome in many who have normal hearts Women have been found to predominate in the cases studied by Edwards and White[80] In a series of 5000 consecutive private cases these observers report a definite diagnosis of neurocirculatory asthenia in 13 7 per cent The majority of their patients (85 8 per cent) were under 50 years of age

Twenty five years ago at the outbreak of the first World War the symptoms observed in the effort syndrome group were thought to represent the early warnings of various disease states However the years have passed and hypertension and hyperthyroidism have not appeared in excess of the expected ratio in the groups that have been followed With the world again at war the number of cases will increase because the provocative factors of fear hunger and exhaustion are certain to reappear Recurrence of the symptoms in the same persons is not unlikely since the basic constitutional factors producing them still exist

Neurocirculatory asthenia occurs more often in individuals with perfectly normal hearts (65 2 per cent of White s series) but there is nothing to prevent its occurrence in those with heart disease (19 6 per cent of White s series) who possess unstable neurotic personalities In the latter group the signs of an organic cardiac lesion will be recognized but the examiner will be struck at once by the exaggerated character of the symptoms when viewed in the light of the amount of demonstrable cardiac damage Rheumatic heart disease is the type most likely to be complicated by neurocirculatory asthenia

MANAGEMENT

The management of the patient with true neurocirculatory asthenia is by no means easy However the earlier the condition is detected in army practice and proper treatment begun the quicker will the soldier be able to return to full duty Removal from the front line is usually in itself sufficient to produce some degree of improvement particularly if rest is the first measure employed Tension is relieved better hygienic surroundings prevail, and these factors at once favor convalescence

The first essential in treatment is to give the patient an honest statement of the exact status of his case This takes time He must be shown

the result of the thorough physical examination including electrocardiogram and orthodiagram, and its significance explained He must be told that there is no evidence of heart disease, but that the annoying and incapacitating symptoms have appeared because he has shown a lack of training Health he must be made to realize will be regained by a process of training and exercise is in order not bed rest The type and duration should fit each case (Chapter 20) Individual care while not possible in the army where the exercises are carried out in groups is possible in civilian practice and leads to a quicker result than mass handling

**Regime** The patient s day should be planned with care and the program written out during the consultation No deviations should be allowed The number of hours of rest at night should be specified coffee tea tobacco and alcohol forbidden and the strenuous features of the daily work at first prohibited The patient must realize the importance of starting treatment on a much curtailed schedule even though this attracts the attention of coworkers to him At all costs he must be launched on an exercise allowance that he is capable of maintaining and this can be gradually increased according to the response shown at subsequent visits Exercise is always prescribed in a precise manner and amounts raised as tolerance is acquired

**The general physical examination** may reveal some foci of infection in teeth tonsils sinuses or prostate These should be evaluated (page 440) and any other abnormality present should receive appropriate attention Tuberculous infection calls for special management

**Use of Drugs** As far as compatible with good practice drugs should be avoided but if needed in the treatment of neurocirculatory asthenia they should be directed toward the minor complicating symptoms like headache constipation etc As far as the condition of neurocirculatory asthenia itself is concerned drugs are of little value The patient should be made to realize the cause of his condition then the fewer drugs used in the treatment the better Digitalis accentuates the symptoms particularly the palpitation and should not be used If secondary anemia is found iron and the usual dietary measures may be prescribed at the start of treatment

**Re examination** of the patient at intervals is justified to make sure that the diagnosis originally advanced remains correct Heart size following additions to the exercise prescription should be determined orthodiagraphically and the retrocardiac space viewed on each occasion to rule out the presence of mitral stenosis which is often suspected because of the accentuated character of the first heart sound On the occa ion of one of the follow up visits a basal metabolism determination should be made to eliminate hyperthyroidism as a contributing factor Routine observations of the blood pressure temperature weight and cardiac rate are likewise valuable in directing treatment

Throughout the entire course of therapy the greatest care should be taken to avoid either saying or hinting that any of the symptoms that the

patient describes are imaginary Be prepared to discuss each one at length at any visit If the practitioner does not have time to do this, he should refer the patient for the proper treatment when the diagnosis is established Discouraged and neglected patients generally take their problems and they are real ones to irregular practitioners

### Prevention

Prevention of neurocirculatory asthenia at least of the more severe grades is quite possible during war time if recruits in training camps are efficiently graded upon their arrival Estimation of the capacity to stand certain forms of activity could be ascertained by a schedule of graded exercise prescribed for each new group This sorting-out process is impossible on the basis of physical findings alone although certain clues, previously mentioned are obtained at the first routine examination Lewis [9] has listed some of the graded drills useful in these cases others may be found in Army drill manuals

## ILLUSTRATIVE CASES

### Neurocirculatory Asthenia in the Absence of Signs of Heart Disease

**Case 83** A T an unmarried music teacher of 40 was first examined in October 1937 when she complained of palpitation rapid beating of the heart and dyspnea on moderate exertion She was nervous and apprehensive as a child and avoided activities while at boarding school spending most of her spare time studying music She could not stand much excitement or overexertion Her father died suddenly from what was described to her as heart failure Since his investments had been poor she was obliged following his death to make her own living teaching music She began to worry about finances and lost much sleep She became conscious of her heart action about this time and noticed increased dyspnea and palpitation when walking up the steps to her studio Her pulse would mount to 110 1 0 on climbing one flight of stairs

Examination showed a normal blood pressure measuring 110 systolic and 80 diastolic There was no cardiac enlargement (the orthodiagram showed a small heart of ptotic type) There were no murmurs and the rhythm of the heart was rapid but regular The electrocardiogram blood count and urinalysis were normal

**Discussion** In the first place the background of this patient is suggestive Her school history shows that she was of the frail type inclined to spend more time in the study of music than in developing normal social contacts She was an only child Consequently we should not wonder at the type and severity of the reactions after her father s sudden death Worry loss of sleep and the increase in her activities made necessary by the fact she had to make her own living in a studio some distance from her home precipitated the symptoms of neurocirculatory asthenia She was convinced she had always had a weak heart and the appearance of these marked symptoms on exertion firmly fixed this belief in her mind

Treatment was begun by telling the patient the symptoms she had experienced were indeed real and followed a praiseworthy attempt to make her way against great odds The amount of exertion she had been forced

to expend to open a studio and to renew contacts with many friends in the hope of acquiring pupils was far above her accustomed level Consequently an untrained circulatory system was giving her notice of neglect of exercise that had attended long years at the piano

The result of the examination of the heart was explained in detail and the normal roentgenogram and electrocardiogram were offered as additional evidence She was advised to begin her work on a smaller scale in a studio on the street level Out-of-door exercise in the form of graded walks was prescribed She was encouraged to seek relief from worry in a different home environment where she would not be alone in the evening

No cardiac medication was prescribed A sodium bromide mixture was given for the first two weeks By the end of this time definite improvement was reported The patient was seen at long intervals after this and she stated that all cardiac symptoms were less evident and had ceased to annoy her at all when she was working in the company of friends or attending concerts Considering this patient s build and disposition the background for the reappearance of the symptoms of effort syndrome is ever present so we cannot say she is cured Insomnia overwork or worry might cause their return at any time

### Neurocirculatory Asthenia—Increase in Symptoms Under Medical Management—Relief Following Adrenal Denervation (Presented by Dr James Lehman)

**Case 84** Mr J M age 23 was admitted to the Woman s College Hospital complaining of 'rapid heart beat for the past eight months At times the rate was so rapid that it was impossible to count Precordial pain on slight exertion was added to the picture a month later and he was forced to give up his work as a grocery clerk Upon advice of a physician he went to bed for three weeks and took digitalis He was unimproved After this he was given iodine for a period of two months He gained some weight (six pounds) during this time but felt much worse He was weak, became exhausted on slight exertion and the chest pain and rapidity of cardiac action were still present

Examination revealed a well nourished and well developed adult male who was intelligent and highly cooperative The pupils were equal moderately dilated and reacted to light and in accommodation There was no exophthalmos The thyroid was slightly enlarged The lungs were normal The heart was not enlarged and there were no murmurs The rhythm was regular and the rate varied from 70 to 122 per minute B P was 136/86

Laboratory Data Several urinalyses were normal Hemoglobin was 90 per cent (Sahli) R B C 4 870 000 W B C 6 300 polymorphonuclears 60 per cent lymphocytes 37 per cent monocytes 2 per cent eosinophiles 1 per cent Blood urea was 16 glucose 100 basal metabolic rate was plus four

*Clinical Diagnosis* A *Etiologic* Effort syndrome (neurocirculatory asthenia) B Anatomic No structural disease C Physiologic Normal sinus rhythm D Functional Classification Class I

**Discussion** This young man showed a clinical picture that is typical of neurocirculatory asthenia He was tall and slender and there was marked lordosis The response to slight exertion when he was first seen was exaggerated and consisted of tachycardia breathlessness and chest

pain Great variability of the heart rate was present at all times, a mere change in body position was often sufficient to cause an elevation of the pulse rate of 50 beats a minute Associated with this were tremor shakiness dizziness sweating and excessive fatigue We note that a determination of the blood sugar was normal The fatigue on exertion was following by such a marked *feeling of exhaustion that he was compelled to give up his job* and go to bed at which time all symptoms became much worse Digitalis was certainly not indicated and it is not surprising that no improvement followed its administration

It is interesting to note that iodine was then given a therapeutic trial no doubt with the thought in mind that the condition might in spite of the normal basal metabolic rate be due to overactivity of the thyroid gland There was a slight gain in weight but the symptoms remained the same

Many times neurocirculatory asthenia may appear to simulate thyrotoxicosis but closer inspection of the patient often reveals wide differences *It is very noticeable at the start that the patient with hyperthyroidism* is optimistic and complains very little while the patient with neurocirculatory asthenia is discouraged and constantly complains of many vague symptoms The patient with thyroid overactivity is bold ambitious alert, and moves quickly while the patient with neurocirculatory asthenia is constantly exhausted and moves slowly The appetite is normal or increased in thyroid disease while in effort syndrome, it is poor The skin in hyperthyroidism is warm moist and pink and of unusually fine texture while in neurocirculatory asthenia cold moist (often cyanotic) extremities are seen Even the tachycardia differs in the two conditions When caused by thyroid overaction it is persistent and sustained while in neurocirculatory asthenia it is variable

After many years of research Crile [8 78] has concluded that neurocirculatory asthenia is a pathologic state in which there is an excessive stimulation of the adrenal sympathetic system He has attempted to reduce this adrenal overactivity by denervation of these glands

In our experience adrenal denervation combined with denervation of the aortic plexus or resection of the splanchnic nerves has given gratifying results in a small carefully selected series of cases The operation is attended by little risk and to date there has been no mortality

This patient showed no result following prolonged medical treatment, consequently on 3/31/36 a left adrenal denervation and splanchnic resection were performed The right side was done 4/11/36 The convalescence was smooth except for some abdominal distention The patient was discharged 14 days after the second operation

There was immediate improvement in the heart action this was followed by a gain in weight and strength Later the patient returned to school at the same time working extra hours in the grocery store

On 12/29/36 a gain of 15 pounds was reported The pulse was 76 B P 130/90 At the time of this visit he was attending school and working during week ends There was no recurrence of rapid heart action

1/28/37 The patient reported a gain of three additional pounds The pulse was 80 B P 130/80 No symptoms

On 5/13/39 the patient stated that he was working every day in an office There were no symptoms Activities had been gradually increased in fact he was able to play tennis occasionally

## PSYCHONEUROSIS

The beginning of health is to know the disease CERVANTES *Don Quixote* Pt 11 Ch 60

Symptoms referable to the cardiac mechanism may develop in psychoneuroses of any type Those most frequently involved are the fatigue neuroses (neurasthenia) and the introspective neuroses (hypochondria) Anxiety states have cardiovascular symptoms which are apt to be built around chest pain or cardiac palpitation Substitution neuroses (hysteria) or obsession states (psychasthenia) less often present cardiac problems

### ETIOLOGY

Psychoneurotic states occur in patients with established heart disease as well as in normal individuals The remark of a medical examiner concerning the presence of a heart murmur may first direct attention to the heart The adventitious sound in question may be and indeed often is entirely functional yet fixation is established and the patient is started on the road to invalidism The road back if there is one is long and difficult It is just as grave an error to diagnose heart disease on the basis of a functional murmur as it is to miss the diagnosis of an early organic lesion Hasty decisions rendered in dispensary or office in regard to cardiac disease are unfortunately at the bottom of many of the cardiac psychoneuroses Although the patient s story may sound typical of neurosis a careful and complete cardiac study should be made before an opinion is rendered Snap judgment is always dangerous

The present-day tendency on the part of newspapers to acquaint the public with many facts concerning heart disease commendable as it may be is not without serious drawbacks Too much attention often is paid to symptoms of little importance by a large group of potential psychoneurotics who are unable to sort the wheat from the chaff The health talk many times serves to establish firmly the idea of heart trouble because the description always seems to fit The sudden death of a near relative from heart disease may kindle fear and start the neurotic on the rounds of physicians offices Pain caused by any thoracic or abdominal disorder and referred to the upper abdomen or chest may be the innocent cause of much needless alarm Given the proper soil a host of incidents is capable of establishing fixation on the cardiac apparatus Often symptoms having their origin outside the heart may be responsible Since the heart of all organs in the body commands the most attention a fear of sudden death

arises when pain in the chest or any abnormality of cardiac rate or rhythm probably in themselves innocuous force their way into conscious perception The fear of heart disease becomes deep rooted and is difficult to dislodge

### Diagnosis

It is always well to allow the patient with a functional heart ailment to tell his own story in his own way without interruption This privilege will contribute greatly to the diagnosis since the psychoneurotic individual usually will describe a multiplicity of symptoms If there is fixation on chest pain the story the patient presents may often be the perfect description of angina acquired as a result of much travel in medical circles However when questioned there will generally be some small detail of the account that will not fit the picture the relationship of the pain to exertion its radiation or the presence of precordial tenderness

**Palpitation** is a common cardiac complaint among psychoneurotics sometimes dating back to a scare in childhood The fear produced by the original accident is at once recalled whenever palpitation occurs Soon the patient becomes acutely conscious of the heart action and is quite convinced that serious organic heart disease is present Advice delivered over the radio at this point is no help The occurrence of premature beats or extrasystoles while harmless increases the introspection and the psychoneurosis becomes more deeply rooted These patients may describe every skip of the heart for a 24 hour period (Case 69) a symptom in itself quite suggestive of psychoneurosis

**Other Symptoms** While precordial pain tachycardia, and palpitation are most commonly complained of any of the symptoms of cardiac disease may be presented as the chief complaint by a psychoneurotic individual Dyspnea even the nocturnal variety may be described in addition to fainting vertigo coldness of hands and feet and a sense of suffocation A thorough deliberate physical examination at the start impresses the patient and will satisfy the examiner that organic heart disease is absent It is important to avoid haste in this initial study in order that the slightest detail will not be omitted for the average psychoneurotic patient is well informed concerning the procedures to be expected as part of a modern cardiovascular examination During the course of auscultation the physician is closely watched consequently it is wise not to pause too long in any area If a systolic apical murmur is present in a rapid overactive heart which often accompanies the psychoneurotic state, it is wise not to pay too much attention to it If the patient has previously been informed of its presence he will usually tell the physician when this stage of the examination is reached It is best to defer answering questions concerning any of the signs elicited until the entire study has been finished The importance of the systolic murmur can then be stated in the summary

**Successful treatment** of cardiac symptoms that are a part of a psychoneurosis is difficult and many times it will require the skilled services of a

psychiatrist If the physician undertakes to treat one of these patients he must realize at the start that it is a time consuming procedure and if he does not have sufficient time and interest he should refer the patient to another physician

At the initial interview, the patient should be encouraged to tell his own story Much can be accomplished in an atmosphere where hurry is not evident if a sympathetic and encouraging attitude is adopted by the physician Otherwise he is not likely to hear the whole story and perti nent details may be withheld Let the patient have his say Make no attempt to have the story related so as to follow a convenient form Such a history may be useful for filing but in the end it generally contains a conglomeration of facts that lead nowhere In addition many patients will hesitate to relate the whole story of an illness when they notice that every thing is being taken down by the physician

When the history and physical examination are finished the physician should tell the patient that he has cardiac symptoms but that the cause is evident and complete cure is possible It is obvious that a definite state ment like this cannot be effective unless the full confidence of the patient has been gained by a careful and painstaking examination

Usually a search through the data will reveal the cause of the heart attacks in some emotional incident Emphasizing this association and giving the patient the necessary encouragement successfully launches the cure Similar incidents may then less readily provoke symptoms Im provement may be expected to follow in a few weeks In all doubtful cases and in those where response is not evident in a reasonable time the opinion of a psychiatrist should be obtained

## ILLUSTRATIVE CASES

### Cardiac Psychoneurosis Complicating Rheumatic Heart Disease

**Case 85** Miss A M a single American clerk of 25 was first seen in June 1936 There was no previous rheumatic history or illness of any nature On insurance examina tion the month before a heart murmur was discovered and the patient was informed that she had heart trouble Since then she developed dyspnea palpitation weakness vertigo insomnia and a catch in her breathing (*sighing respiration?*) She began to miss many days at work and when examined was contemplating resigning her position She expressed the fear of sudden death

Physical Examination showed a blood pressure of 120/80 very slight cardiac enlargement a presystolic *murmur* and accentuated first sound over the region of the apex The electrocardiogram showed right axis deviation and notched P waves in leads and 3 An orthodiagram showed mitralization and slight congestion in the hilar regions on both sides There were present superficial and deep tenderness in the left precordial area

Clinical Diagnosis A Etiologic Rheumatic Psychoneurosis B Anatomic Cardiac enlargement Mitral stenosis Mitral insufficiency C Physiologic Normal sinus rhythm D Functional Classification Class 1

**Discussion** There is no doubt that this girl had a well established mitral stenosis unrecognized until the time of the insurance examination

When this fact was communicated to her she at once associated it with *sudden death* She was a *hypersensitive nervous individual already* possessing the mechanism necessary for the development of a psychoneurosis The statement of the insurance examiner was the precipitating factor Some physicians are of the opinion that the diagnosis of psychoneurosis should be advanced only when the physical examination and laboratory studies are entirely negative However, this is far from the case in many instances as this patient shows

The physician who examined this girl mentioned the heart murmur and advised her to consult her own physician To be sure his advice would be followed he laid too much emphasis on the gravity of the situation as a whole

At the start of the treatment of an uncomplicated psychoneurosis an explanation of the symptoms experienced by the patient is easy, but the task becomes more difficult when there is a background of organic heart disease It should however be attempted The care necessary for the existing lesion should also be stated and the good reserve strength of the heart muscle demonstrated Most of these patients when first seen have been given digitalis some in large doses The withdrawal of this drug may be stressed to drive home the statement that the heart muscle although damaged has sufficient reserve which can be retained for many years

Schnur[331] has recently suggested as a therapeutic test for differentiating the symptoms of cardiac psychoneurosis from those of organic heart disease the injection of novocaine intradermally at the affected site The hyperalgesia tenderness and pain disappear at once *Often the symptoms* of the psychoneurotic state will be relieved by this procedure Pain due to organic heart disease will not be relieved by this method

Harmless arrhythmias many times may precipitate a cardiac neurosis In instances where the arrhythmia appears following trauma it may continue to produce symptoms in spite of all therapeutic effort until a legal settlement has been made The patient whose history appears in Case 69 showed improvement following small doses of quinidine sulfate, a sedative mixture and increase in the prescription of out of door exercise

In some patients over 40 years of age the precordial pain that attends frequently recurring premature beats may be misinterpreted as the anginal type The patient may hear of this in which event it serves to augment the symptoms of the psychoneurosis

These patients should be completely examined at the start and all tests made A large dose of reassurance should then be administered and at subsequent visits the patient should be advised and educated Repetition of an entire physical examination or special examinations in these cases at too frequent intervals serves to make the patient suspect he was not told the truth at first Opinions rendered must be positive to be of value Advice at the end of the interview 'to take things easy' wastes the time spent before this remark for the patient usually cannot link this advice with the previous statement that he has a perfectly normal heart

### Cardiac Psychoneurosis During the Course of Coronary Disease

**Case 86** G C a Hebrew tailor of 54 was first seen in January 1934 Three months before he had an attack of severe chest pain which was proved on electrocardiographic study to be caused by a posterior coronary occlusion He remained in good condition clinically and the laboratory studies pointed to progress in the healing of the area of infarction However his complaints were multiple pain in the left shoulder recurring transient pains over the precordium insomnia vertigo epigastric and substernal burning and fear of sudden death

Physical examination showed B P 1 0/80 no cardiac enlargement a soft systolic apical murmur There were areas of superficial and deep tenderness over the precordium

Clinical diagnosis A Etiologic Arteriosclerosis Psychoneurosis B Anatomic No cardiac enlargement Coronary sclerosis Cardiac infarction C Physiologic Anginal syndrome D Functional Classification Class 3 Therapeutic Classification C

**Discussion** The coronary occlusion affected an area of cardiac muscle in this patient producing an infarction which healed satisfactorily This event had a marked effect on the nervous system precipitating a typical psychoneurosis which was the cause of the prolongation of the symptoms In the presence of a serious organic lesion of this nature many physicians are hesitant in considering any of the symptoms that may be subsequently presented as functional when the initial findings point conclusively to a serious heart disorder However all the pains in the chest complained of by this patient could not have been due to small occlusions At least frequent electrocardiograms did not show them Neither could we assume that these atypical pains were anginal They did not respond to nitroglycerine on all occasions and associated with them we had to consider the man s personality race and the presence of areas of hyperalgesia and deep tenderness over the precordium

The first problem here was to discuss the situation frankly with the patient and his family and write down a graded system of increased activities with the aim of dislodging the patient from bed where he had been invalided for too long a period His pains were not made worse by the end of the first week on the new program Consequently his allowance was increased during the second week At the end of this period his condition continued to improve so he was allowed to return to his shop in a supervisory capacity beside the cash register After this his complaints were few His medication consisted of a capsule containing 15 mg (¼ grain) of phenobarbital and 0 2 Gm (3 grains) of theophylline ethylene diamine after meals

### Cardiac Psychoneurosis and Congenital Heart Disease

**Case 87** Mrs C A a housewife of 30 was first seen in December 1933 when she complained of precordial distress weakness vertigo and insomnia She was emotionally unstable wept easily and profusely at the slightest provocation The family history was suggestive The only child a daughter of ten was an imbecile The patient stated that she had always been weak because of heart disease at birth She was not a blue baby but the family physician told her mother that she had a leaking heart

Physical examination showed slight cardiac enlargement a systolic thrill in the third left interspace accompanied by a high pitched systolic murmur The fingers re

not clubbed and no other defects were noted on physical examination The electrocardiogram showed high voltage of the QRS groups

**Discussion** Cardiac psychoneurosis when associated with organic heart disease will usually be found complicating coronary, rheumatic or hyper tensive types since these are the most prevalent It is rarely seen combined with congenital heart disease because of the infrequency of congenital defects in the cases seen in practice

This patient was a typical psychoneurotic individual The idea of heart disease became firmly fixed in her mind at an early age In consequence she always led a sheltered secluded life at school and at home Her mother presented a similar problem in neurosis and was treated for the combination which causes most practitioners to seek shelter essential hypertension chronic arthritis and mucous colitis The patient took little or no exercise She was carried up the stairs as a child and always lived in a first floor apartment during married life Obesity developed in later years and thus accentuated the dyspnea that appeared on slight exertion The psychoneurosis was so deep-seated that the usual measures over a considerable period were ineffectual in bringing any measure of relief The signs of her lesion were so typical and the family history appearance and actions so characteristic of the superimposed psychoneurotic state that this patient was used for clinic demonstration on frequent occasions The last time she was shown the complaints of weakness malaise and slight fever failed to attract the attention of the clinician When the patient failed to reappear for the next examination our social worker traced her to the ward of another hospital The diagnosis of subacute bacterial endocarditis had been established by positive blood culture *

The lesson to be learned here is never to neglect to follow up the new symptoms that appear even though the diagnosis of psychoneurosis has been previously established It is also important not to overlook the possibility of the more common complications that attend the cardiac lesion

* Autopsy findings Large (uncomplicated) interventricular septal defect containing the vegetations typical of subacute bacterial endocarditis (Courtesy of Dr George C Griffith )

# 14

# MISCELLANEOUS TYPES

Up to this point we have considered the main features and the management of various etiologic types of heart disease (page 60) The majority of the remaining conditions will be rarely encountered by the practitioner and our present knowledge of the other types is still far from complete Consequently brief descriptions of this miscellaneous group that includes the influence of anemia neoplasms pulmonary disease hypotension other infections and toxic agents on the heart although entirely unrelated will be grouped for convenience in this chapter Since most of the cases where cardiac trauma is suspected are seen with the surgeon the discussion of this subject has been placed in Chapter 17

## ANEMIA

In the presence of severe anemia any changes observed in the heart on physical examination should be interpreted with care for when the hemoglobin falls below 50 per cent symptoms closely simulating heart disease may appear The circulation time is decreased in anemia while the cardiac output and the minute volume show an increase These changes may be regarded as safety mechanisms to bring the amount of oxygen transported to the tissues nearer the normal level

The heart muscle in anemia is flabby and shows the familiar tiger markings chiefly in the left ventricle (Fig 147) Of 23 cases of Addisonian anemia reported by Cabot[49] hypertrophy and dilatation were observed at necropsy in 22 which agrees with other reports that an increase in heart size is present in advanced anemic states (chlorosis secondary anemia primary pernicious anemia) Cardiac enlargement has also been observed following the experimental production of anemia in animals

### Symptoms

The symptoms induced by anemia are breathlessness vertigo palpitation weakness and at times anginal pain on exertion Likewise a lessening of the blood supply to the legs particularly if some degree of sclerosis already exists may produce intermittent claudication The cause of both types of pain is muscle anoxemia Cabot reported three cases of typical angina associated with pernicious anemia in patients who at autopsy showed no coronary change In each instance the pain was produced by exertion and relieved by rest If advanced coronary disease is absent complete relief of the angina is possible in these cases following intensive treatment of the anemia and improvement in the blood count

SIGNS

In advanced anemia, cardiac enlargement may be evident on percussion The heart sounds are usually weak Systolic murmurs are often present in the region of the apex and at the base and their quality differs in no respect from those murmurs heard in patients who have actual valvular disease The murmur at the apex is considered to be secondary to a relative dilatation of the mitral ring with the production of mitral regurgitation

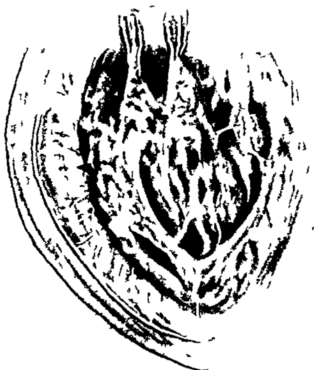


FIG 147 Tiger mottling in anemia

Dilatation of the aorta and pulmonary artery may be accompanied by murmurs in these areas In severe cases diastolic murmurs have been described Consequently considerable care must be taken in anemic individuals to avoid making the diagnosis of heart disease since the murmurs of anemia may simulate mitral stenosis Advanced untreated anemia may ultimately cause congestive manifestations as Cabot s *series of autopsied* cases have demonstrated However, where breaks in compensation have occurred pre existing heart disease of another type has usually been the cause, the anemia merely adding the final load that precipitates cardiac failure

When asphyxial blood is perfused through the coronary arteries it produces changes in the electrocardiogram similar to those seen when a coronary vessel is clamped Such evidence suggests that the changes brought about by anemia may be confused with those that arise secondary to a coronary occlusion In these instances it has been suggested that the change in the RS T interval in anemia is caused by a high concentration of locally produced metabolites

### Management

When the anemia is controlled all cardiac signs and symptoms may disappear The heart size if determined by accurate methods will be found to be smaller The various murmurs may no longer be heard and the anginal pain is no longer experienced Even in the presence of coronary disease improvement in the blood picture may often sufficiently raise the threshold to pain on ordinary exertion Re examination of a number of patients efficiently treated for progressive pernicious anemia after the blood count is normal reveals only the signs of cardiovascular disease that one would expect to encounter in any similar group of patients at the same age period

## PULMONARY HEART DISEASE
## (Cor Pulmonale)

Increase of pressure in the systemic circulation is followed sooner or later by hypertrophy of the left ventricle and hypertensive heart disease follows If the pressure in the pulmonary circulation is increased either suddenly by a large pulmonary embolism or failure of the left ventricle or more gradually by mitral disease or chronic pulmonary fibrosis we speak of the resulting condition as cor pulmonale or pulmonary heart disease

### Acute Cor Pulmonale

#### ETIOLOGY

The sudden right ventricular strain and dilatation that follows a large pulmonary embolus has been designated acute cor pulmonale by McGinn and White [46] Death in Case 29 was hastened by the rupture of an aortic aneurysm into the pulmonary artery and the sudden increase in the pressure in the lesser circulation Venous thrombosis following operative procedures has been *shown to be the most common source of the emboli* causing acute cor pulmonale

#### SYMPTOMS AND SIGNS

The production of acute cor pulmonale requires the blocking of at least 60 per cent of the pulmonary arterial circulation The symptoms are sudden in onset and consist of severe chest pain and dyspnea these are

usually quickly followed by signs of shock Death very often occurs suddenly after a massive occlusion of one of the main branches of the pulmonary artery while after a less extensive obstruction, survival may be attended by signs of right sided cardiac failure Cardiac size may increase particularly to the right, and venous engorgement may appear Electrocardiographic alterations resembling those produced by acute coronary occlusion may be observed but unlike those produced by coronary accidents the changes brought about by pulmonary embolism usually fade in a few days as balance is restored (see Fig 251)

The management of acute cor pulmonale has been included under the cardiac emergencies (page 509)

## Chronic Cor Pulmonale

The gradual replacement of lung areas by scar tissue and the obliteration of many branches of the pulmonary artery produces in some cases an interference with the blood flow Consequently a strain is placed upon the right ventricle and in time hypertrophy develops and later a right sided heart failure may appear

### ETIOLOGY

Chronic cor pulmonale may be secondary to a number of diseases of the lung Emphysema tuberculosis and pneumoconiosis commonly produce it while primary pulmonary endarteritis obliterans (Ayerza s disease) a rare condition is invariably accompanied by the signs of chronic pulmonary heart disease Chest deformities may place a strain on the right ventricle while metastatic carcinomatous infiltration of pulmonary arterioles may produce the same effect in some cases

*Chronic cor pulmonale may develop at any age* *Since the lesions most* apt to initiate the process occur in older people, most of the instances encountered clinically fall in these groups Primary pulmonary arteritis however often occurs in younger patients

Enlargement of the right ventricle dilatation of the pulmonary artery, and an increase in size of the right auricle are the main pathologic changes that occur in the heart Elevated pressure in the pulmonary circuit may also lead to atheroma of these vessels This condition however must not be confused with the change that takes place in the endothelium in cases of pulmonary endarteritis obliterans

### SYMPTOMS

The symptoms of chronic cor pulmonale are those of the underlying pulmonary disease in addition to the symptoms that result from strain and failure of the right side of the heart Dyspnea cyanosis hemoptysis clubbing of the fingers and toes may be secondary to the pulmonary disease Polycythemia often appears The signs and symptoms that direct attention to the heart are venous engorgement, the typical cardiac silhouette (see Fig 148A) the accentuation of the pulmonic second sound

and at times a pulmonic systolic murmur Extreme cyanosis ("black cardiacs ) accompanies advanced degrees of pulmonary sclerosis that may occur in some cases of chronic cor pulmonale Arrhythmias do not very often complicate the picture

### DIAGNOSIS

A bedside demonstration of right ventricular enlargement is difficult in these patients owing to the low diaphragm and the emphysema The right ventricle moreover faces anteriorly and changes in its size tend to produce alterations that are not appreciated by percussion The electrocardiogram in pulmonary heart disease shows a right axis deviation (see Fig 148B) and for this reason is valuable in diagnosis

The problem of differentiating between symptoms of pulmonary origin and those caused by cardiac insufficiency often arises Additional laboratory tests may be valuable in helping the clinician out of this difficulty The most useful of these are the measurement of the venous pressure and the arm to lung time (ether method) and the lung to tongue time (decholin method minus the ether time) [87] Abnormal circulatory measurements point to myocardial failure

In contrast to acute cor pulmonale the chronic form may show a slow progression over a number of years Resistance to pneumonia is generally poor consequently this disease takes a heavy toll particularly among old people Circulatory failure is also a common cause of death and is apt to follow a chronic course The prognosis in most cases depends upon the nature of the underlying pulmonary or cardiac lesion

### MANAGEMENT

The general plan of management is based upon the nature of the disturbance giving rise to the cor pulmonale When heart failure appears the usual measures are employed including rest digitalis and diuretics (page 74) If cyanosis deepens oxygen is useful (page 96)

A further discussion of the effect of asthma on the heart and the treatment of asthma complicating heart disease will be found in Chapter 16

## ILLUSTRATIVE CASE

### Chronic Pulmonary Heart Disease (Cor Pulmonale) Secondary to Bronchial Asthma of Long Duration

**Case 88** E W a salesman of 43 was first seen in August 1938 complaining of shortness of breath and cough Frequent attacks of asthma following respiratory infections had been present since childhood Cough was continuous for the past ten years increasing in severity during the winter Dyspnea was marked

Physical examination showed cyanosis and emphysema The heart sounds were distant and regular Rate 100 No murmurs were heard B P 110/80 The liver was palpable and tender a few centimeters below the right costal margin Slight ankle edema

Laboratory Data The electrocardiogram showed a right axis deviation (Fig 148B) The roentgenogram showed cardiac enlargement and an increase in the region of the

pulmonary conus (Fig 148 A) There was also enlargement in the region of the right ventricle The Wassermann was negative The blood count showed R B C 5 700 000 and W B C 9 00

CLINICAL DIAGNOSIS A Etiologic Chronic cor pulmonale secondary to bronchial asthma B Anatomic Cardiac enlargement C Physiologic Normal sinus rhythm



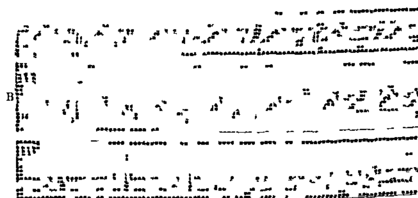




FIG 148 A Roentgenogram Note dilatation of pulmonic conus B The electrocardiogram Note presence of right axis deviation

Early (right sided) cardiac failure D Functional Classification Class 3 Therapeutic Classification Class C

**Discussion** The history of attacks of asthma for many years and the marked emphysema discovered on physical examination in this patient furnish the necessary background for the diagnosis of chronic cor pul

monale The presence of right sided heart failure was indicated by the cyanosis engorged jugulars large liver and peripheral edema The roentgenogram and the electrocardiogram completed the picture

The precipitating cause of the failure was not evident from the history It may have followed the most recent upper respiratory infection Treatment was directed toward the cardiac failure and bed rest and digitalis were prescribed Digitalization was accomplished in one week but the cough continued Ammonium chloride in 1 0 Gm (15 grains) doses was given every four hours and codeine sulfate 30 mg (½ grain) was useful on a few occasions at night During the second week much relief was obtained from two intravenous injections of mercupurin (2 cc ) at five day intervals although at the time they were given no edema was evident

The patient was allowed to be out of bed at the end of the second week Digitalis maintenance dosage was continued and at the beginning of the third week he was referred for study of his bronchial asthma (page 462) Since he was local agent for a steamship company he was advised to seek transfer to a branch office in the south where better climatic conditions were known to prevail

## TUMORS

Tumors of the heart and pericardium are very rarely the cause of cardiovascular symptoms All too often they are discovered by the pathologist when the possibility of their presence was not even considered by the clinician On reviewing the rather extensive literature on the subject we note that every kind of tumor may involve both heart and pericardium Secondary metastatic growths are much more common and can invade the heart from almost any location in the body Primary growth both benign and malignant types likewise have been reported

### Types

**Primary Growths** About 80 per cent of all primary tumors that invade the heart are benign myomas while the malignant tumors are nearly always sarcomas The benign tumors have been known to arise from the auricles (usually the left) and interauricular septum and the malignant tumors while also showing predilection for the auricles as a site of origin are usually found on the right side The reason is unknown[4] Many of the tumors are pedunculated (see Fig 146) and fill the heart cavity from which they take their origin Some have been found to break off and act as ball valves Others may invade and replace the myocardial structures or may involve the pericardium and compress the heart The conduction system may also be affected and heart block produced (see Case 81)

**Secondary involvement** of the heart by a malignant growth may occur as part of a widespread dissemination or by extension from a

neighboring organ The tumor cells generally reach the heart by way of the blood stream the lymphatic channels playing a much less important role Carcinomatous metastases to the heart are more common than sarcomatous but both occur

Metastatic growths may arise from any part of the heart but the right side is more often and more extensively involved than the left The activity of the heart often prevents metastatic growths Later if these processes do gain a foothold their growth is slow, and the heart may compensate for either invasion or compression for a long time When cardiac failure does occur in the absence of a satisfactory etiologic explanation particularly if a malignant process has been previously demonstrated in any organ of the body the possibility of tumor of the heart or pericardium should be kept in mind

## ILLUSTRATIVE CASES

### Cardiac Compression and Failure Following Metastatic Tumor Infiltration—Autopsy

**Case 89** G W a Polish American mechanic of 51 was admitted to the Philadelphia General Hospital on November 9 1938 complaining of cough hoarseness dyspnea and swelling of the feet

History Symptoms appeared four weeks prior to admission when the cough that had been present for 0 years became more severe and was followed by persisting hoarseness Shortness of breath was noted about this time increasing to orthopnea on admission Edema of the feet at night was present four weeks before entry On admission this had advanced to the lower sacral region Past medical family and social histories were negative

Physical examination A thin cyanotic white male B P 94/60 Veins of the neck engorged as well as the veins of the axilla and anterior chest wall Trachea in the midline Chest emphysematous Dulness to percussion over both lung bases Coarse musical inspiratory rales heard over both sides Left cardiac border 14 0 cm to the left of the midsternal line in the sixth interspace Heart sounds weak and distant No murmurs Rhythm regular Liver edge at umbilicus Pitting edema of the lower extremities

Laboratory Data All urine examinations were negative Kahn negative Blood count hemoglobin 78 per cent (Sahli) R B C 4 00 000; W B C 7 00 differential normal Sputum negative for tubercle bacilli

The electrocardiogram (Fig 149B) showed diminution of the amplitude of the QRS complexes

Bronchoscopic examinations showed paralysis of the left vocal cord extrinsic in type There was no evidence of malignancy in the bronchial tree

Roentgen examinations (Fig 149A) (A) the initial study showed a dilated and enlarged heart and fluid in both lung bases (B) three weeks later showed a smaller heart less pulmonary congestion and a large pulmonary conus (C) taken six weeks later showed a diffuse haziness over the left lower hemithorax The left cardiac border was blurred with considerable dense fuzziness about the left hilum Roentgen diagnosis Mediastinal adenopathy, most likely malignant displacing the heart

Clinical Diagnosis A Etiologic Metastatic tumor Cardiac compression (?) B Anatomic Cardiac enlargement C Physiologic Congestive failure due to cardiac compression Normal sinus rhythm D Functional Classification Class 4 Therapeutic Classification Class E

AUTOPSY Ostia and valves unchanged Upper sections of the myocardium were densely infiltrated by tumor The whole thoracic cavity seemed to be crowded by a large tumor mass The layers of the pericardium were involved by the growth and could not be separated The tumor was nodular yellowish hite in color and very firm in cons stency The large vessels of the mediastinum were patent The microscopic sections showed the invasion of the myocardial structure by the tumor cells There was a primary carcinoma of the lung with metastas s to regional lymph nodes and liver as well as the extensions to the pericardium and myocardium

DISCUSSION The increasing dyspnea weakness and cough complained of by the patient centered all attention on the cardiovascular system and




FIG 149 A Roentgen stud es 1 November 14 1938 2 December 7 1938 3 January 1939 For explanation see text (Courtesy X Ray Department, Philadelphia General Hospital) B The electrocardiogram Note decreased voltage of the QRS groups and depress on of S-T intervals in leads and 3

he was admitted to the hospital as a case of cardiac decompensation Further study however revealed no cause for the failure Finally the aphonia and the nodule observed on the left border of the roentgenogram in the region of the pulmonary artery in the absence of mitral disease

shifted attention from the heart A neoplasm was suspected but from the data available its primary location and exact nature remained obscure

In carcinoma of the lung the possibility of cardiac and pericardial invasion must not be overlooked In a recent study of 1082 cases of malignant disease coming to autopsy Scott and Garvin[337] reported metastasis to the heart and pericardium in 118 or 10 9 per cent Carcinoma of the bronchus and breast made up 48 per cent of these cases In this patient the growth extended from the bronchus and completely encased the heart Invasion of the cardiac structures next took place and practically no myocardium remained (Fig 150) It is remarkable how the residual amount of cardiac structure was capable of sustaining life in this patient for so long a time Interference with diastolic filling finally caused death

Rarely the invasion of the heart by a metastatic tumor growth may involve the conduction system and attract attention to the heart (see Case 81) Although few cases of tumor of the heart are diagnosed correctly prior to autopsy the condition should at least be suspected in the presence of unexplained cardiac failure or heart block significant alterations in the roentgenogram collections of hemorrhagic fluid in the pleural or pericardial cavities or any other cardiac abnormality in a patient recently treated for a malignant process anywhere in the body but particularly in the lung or breast

## Metastatic Growth in Right Auricle and Ventricle from Sarcoma of the Knee—Autopsy

**Case 90** M M a negress of 60 entered the Philadelphia General Hospital complaining of pain in the left leg for five years For the past four years she had lost all motion in the limb and for the past two months had noticed a hard lump on the outer aspect of the left knee the lump had grown rapidly just prior to admission No other symptoms were present

Physical Examination B P 140/90 Rhythm regular rate rapid No murmurs Breath sounds were harsh at the right base and a few scattered rales were present A firm hard mass adherent to the underlying structures was present just above the left knee

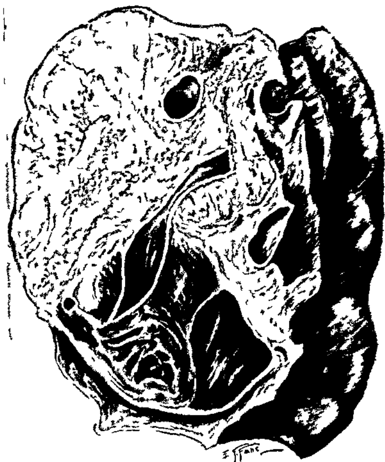
Laboratory Data Wassermann negative Roentgenogram size of the heart shadow was increased with prominence of the pulmonary conus No evidence of metastasis in the lungs Roentgenogram of the leg showed a circular mass in the soft tissues of the lower quarter of the left femur Posterior to the femur in the soft tissues were several dense irregular shadows

The urine on several occasions was negative and the blood count was normal

Autopsy The right auricular appendage contained a growth a long tail of which descended as far as the anterior cusp of the valve The upper and outer portions of the right ventricle were involved in a large mass of growth which extended into the cardiac chamber in the form of polypoid masses The lungs showed metastatic sarcoma

**Discussion** Infiltration of the right auricle and ventricle occurred in this patient and no symptoms were present to direct attention to the heart The only findings were a slight increase in heart size and increase in the prominence of the pulmonary conus in the roentgen picture

The tendency of sarcomatous growths to infiltrate the heart walls and encroach upon the cavity of the heart by the formation of polypoid




F[illegible] 150 W[illegible] [illegible] k[illegible]tch [illegible] [illegible] [illegible] f[illegible] [illegible] tu[illegible] (Fr[illegible] n[illegible] [illegible] Cl[illegible]n[illegible]

growths is seen in this case (Fig 151) The heart valves were not involved although very rare cases have been reported where tumor cells grow upon the valves simulating subacute bacterial endocarditis

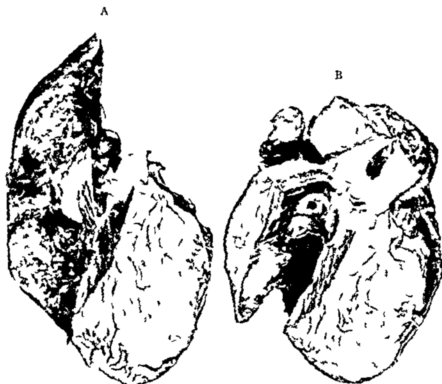



FIG 151 A Tumor growth in right auricular appendage B Invasion of wall of right ventricle A small polypoid growth extended into the right ventricular chamber

## HYPOTENSION

So often patients are seen who complain only of low blood pressure When questioned further the fact is usually brought to light that symptoms began when the diagnosis was made by a physician at the time of a check up for life insurance or an examination for some trivial ailment Complaints of a varied nature are laid at the door of low blood pressure and a great deal of medicine is consumed in attempts to elevate it to a respectable level Many times there is a tendency to lose sight of the fact that low blood pressure is after all not a disease In most instances it is harmless unless mis statements concerning its importance become firmly fixed in the imagination Every physician sees many robust and healthy patients who have systolic pressures of 100 mm of mercury or less

SYMPTOMS AND SIGNS

On the other hand individuals of the asthenic type may be encountered in clinic and private practice who complain of weakness vertigo headache, palpitation and vague digestive tract disturbances They, too may blame their low blood pressure' for every symptom but again we cannot regard the matter as definitely proved, for the low blood pressure may be just as much a part of the picture as the visceroptosis or the small heart There is no reason to believe that the low blood pressure per se accounts for all the complaints and no reason to treat this group as 'essential hypotension

ETIOLOGY

Hypotension may be secondary to a number of important conditions For example we meet it quite often during the course of acute infectious diseases Certain chronic conditions like tuberculosis are also accompanied by arterial hypotension The blood pressure in these instances falls in proportion to the severity of the disease and usually results from the loss of vasomotor tone that accompanies the toxemia The reduction of the blood volume in shock produces a low arterial pressure Myocardial injuries following acute occlusion of the coronary branches are commonly associated with hypotension Various types of endocrine gland disturbances are routinely accompanied by low blood pressure (myxedema Addison s disease) while certain drugs like the nitrite group are capable of producing a sudden lowering of the systemic pressure

**Orthostatic Hypotension** There is an interesting although uncommon condition characterized by sudden fall in the blood pressure when the patient assumes the erect position this may be followed by vertigo faintness and at times collapse I refer to the syndrome orthostatic hypotension Many times patients suffering from this condition will show a decrease in the systolic blood pressure amounting to as much as 50 mm of mercury when they stand There is no compensatory increase in the pulse rate and there is a similar failure of the compensatory mechanism of vasoconstriction which results in an inadequate cerebral blood flow Many normal individuals occasionally experience a sensation of faintness if they suddenly stand erect particularly after a hot bath but this lack of complete circulatory adjustment is not uncommon and should not be diagnosed orthostatic hypotension It differs from orthostatic hypotension in that the circulation makes some attempt to meet the situation The heart rate increases the blood pressure rises at first as the arterioles con strict, but the effort is neither sufficient nor sustained, consequently vertigo and faintness follow the fall in pressure Orthostatic hypotension is caused by a definite impairment in function of the sympathetic nervous system while the faulty circulatory adjustment to the erect posture may occur at some time or another in nearly every normal individual It is mo t often observed during convalescence from acute infectious diseases

### Treatment

The treatment of hypotension consists of appropriate measures directed toward the cause of the symptoms The patient who has occasional vertigo due to a faulty adjustment to postural changes will be little benefited in the long run by continuous dosing with preparations containing drugs of the vasoconstrictor type Measures should be adopted to prevent the pool ing of the blood on the venous side and to increase the return to the right auricle If we follow Nature s suggestion and place the patient in the hori zontal position when abnormal sensations are experienced improvement is prompt and complete For prophylaxis an elastic abdominal belt and stockings of the same material are beneficial During convalescence from acute infectious disease and other prolonged illnesses graded exercise and massage are of value

**Ephedrine and Benzedrine in Orthostatic Hypotension** Relief may be obtained from drugs that have a vasocontrictor effect The members of this group that have proved mo t efficient are ephedrine and benzedrine Ephedrine may be given in 25 to 40 mg doses by mouth every three or four hours but it must be kept in mind that insomnia is a common unto ward effect that follows large doses of this drug Benzedrine in doses of 20 mg at sufficient intervals during the day to give continuous relief is better for routine use but here too insomnia is often complained of by the patient

Allen and Magee emphasize the importance of an individual program of administration of ephedrine in these cases They show that the drop in the blood pressure when the patient assumes the upright position after use of large doses of these drugs is the same However the level of the blood pressure after the drug has been taken is higher and this accounts for the improvement in the symptoms since the low levels that interfere with cerebral flow are not reached Therefore success in the management of these rare cases lies in keeping the blood pressure at a higher level continuously so that when the fall occurs with the change in position the low level will be above the point where symptoms ordinarily occur

The treatment of secondary hypotension is directed toward the main disease The hypotension of shock for example will respond when meas ures are taken to restore the volume of the circulating blood, while in Addison s disease improvement in the blood pressure accompanies the administration of the hormone from the adrenal cortex

## THE HEART IN INFECTIONS

Infections that cause serious alterations in the cardiovascular system are acute and subacute bacterial endocarditis rheumatism and syphilis The remainder are much less important from a cardiac standpoint rarely pro ducing any serious invasion of the heart Many times the circulatory

disturbances that are observed during the course of acute infectious diseases are brought about by failure of the peripheral vascular apparatus

Quite often the effect of fever on the cardiac structure cannot be distinguished from that of the toxins of micro-organisms The cloudy swelling of the heart muscle observed by the pathologist, as well as the more advanced changes that are characterized by cellular infiltration may interfere with myocardial function When these alterations produced by the infectious process affect the blood supply to the myocardium, more important disturbances often result Toxic substances produced by bacterial growth may also attack the conduction system and heart block may suddenly appear during the course of the infection These changes are usually functional and temporary and disappear as the acute infectious process subsides

As a rule, when the course of the acute infection is a short one the heart is able to perform efficiently and few additional symptoms appear If, however the infection is severe or if it is prolonged signs of congestive failure may complicate the picture at any time (page 194) When these signs are accompanied by a feeble rapid pulse a falling blood pressure increase in the heart size and disturbances in rhythm we may suspect a failing myocardium Tachycardia out of proportion to the height of the fever particularly if accompanied by cyanosis is an early sign that usually directs attention to the circulatory apparatus during the course of an acute infection In pneumonia and other pulmonary diseases cyanosis is not in itself a reliable guide but if at any time it is accompanied by falling blood pressure increasing venous pressure and diminution of the pulmonic second sound a right sided heart failure should be suspected The symptoms on the other hand that suggest peripheral circulatory failure are weakness pallor falling blood pressure decreasing pulse pressure tachycardia and faint heart sounds

Murmurs appearing during the course of acute infections are usually caused by temporary myocardial weakness which permits a relaxation of the mitral ring and mitral regurgitation This functional systolic murmur heard over the region of the cardiac apex many times disappears during convalescence from the infection Rarely are these murmurs associated with actual disease of the heart valve unless the disease is of the rheumatic type

## Treatment

An accurate evaluation of the role of the peripheral circulation and of the heart itself in the production of the symptoms should precede treatment Often this may not be possible when symptoms of cardiac and vasomotor failure suggest the presence of both mechanisms

**Caffeine** administered in the form of caffeine with sodium benzoate in 0 5 Gm (7½ grains) doses is a useful remedy in emergencies It may be given intravenously but the injection should be made very slowly and the drug should be well diluted Direct stimulation of the medullary centers produced by caffeine raises the blood pressure and improves vascular

tone It also acts directly on the heart muscle strengthening the systolic contraction and may increase the cardiac output A favorable influence may likewise be exerted on the coronary flow The untoward effects consist of mental excitement and insomnia that are produced in some patients and in the increase in the heart rate If the tachycardia is marked this may decrease diastolic relaxation and result in diminished cardiac output The frequency of the administration of the drug should always depend on the effect it produces and the clinical picture of the patient

**Strychnine** has lost ground in recent years in the treatment of diseases of the cardiovascular system In the opinion of many the drug is worthless unless used hypodermically in large doses that closely approximate the toxic limit In single doses of 0 002 Gm (1/30 grain) to 0 004 Gm (1/15 grain) it increases nerve irritability which may in emergencies result in an increase in the tone of the blood vessels

**Epinephrine hydrochloride** injected intravenously in doses of 0 6 to 1 0 cc causes increased peripheral vasoconstriction and this action can usually be relied upon Intramuscular injections are not as efficient because of the vasoconstriction produced at the site of injection The action of epinephrine should be a continuous one in peripheral circulatory failure hence it is best given combined with 500 cc of physiologic saline or the same volume of 5 per cent glucose by slow intravenous drip (2 cc per minute) Epinephrine acts directly on the vasomotor nerve terminals to produce its constricting effect and through a similar action on the sympathetics to stimulate the heart It should be given with great care in cases where the blood volume has been greatly reduced By increasing the vasoconstriction already produced in these instances it reduces still further the cardiac output by interfering with the return flow of blood to the heart and as Eggleston has pointed out [90] in this manner aggravates the condition for which the drug was given

**Ephedrine and Posterior Pituitary** Both ephedrine and solution of posterior pituitary produce vasoconstriction but are not as certain in their action as epinephrine Administration of ephedrine sulfate in doses of 0 03 Gm (⅜ grain) may be attended by excessive nervousness and insomnia while pituitary extract in repeated doses may be followed by a loss of vasoconstrictor tone and a fall in blood pressure

**Digitalis and strophanthin** should not be given in cases where the peripheral signs predominate Even when frank cardiac failure occurs during the course of the infection digitalis usually has little effect

**Camphor** and the substances possessing a camphor like action such as cardiazol are of little value There may be some stimulation of respiration or a slight reflex effect may occur from irritation at the site of injection but both actions are transient and weak

In all acute infections preventive measures are more valuable than the remedies above described Good nursing proper rest a well balanced diet sufficient fluid intake and if cyanosis appears oxygen by nasal catheter

or tent (page 98) are important in this respect Injections of 50 cc of a 50 per cent glucose solution are helpful When excessive fluid has been lost, the glucose can be given in larger quantities (500 to 1000 cc ) of physiologic saline Blood transfusions under these circumstances are beneficial Great care however should always be used to avoid overloading of the circulation by the injection of too large amounts of fluid When in doubt determination of the venous pressure by the direct method (page 54) may be valuable

DIPHTHERIA

Both the success in the prevention of this disease and the prompt u e of sufficient antitoxin when it does occur make cardiac sequelae rare occurrences today Severe untreated diphtheria however, attacks the myocardium and sudden death in these cases is not unknown The diphtheria toxin causes necrosis of the heart muscle cells and the specialized tissues of the conduction system Arrhythmias produced by invasion of the conduction system furnish clinical evidence of the presence of this destructive process Marked degrees of either auriculo ventricular heart block (page 593) or sinus arrest (page 615) may suddenly appear In addition to the usual clinical signs of heart involvement above described a gallop rhythm may be heard on auscultation furnishing suggestive evidence of prolongation of the conduction time and the toxic state of the myocardium An electrocardiographic study is valuable in revealing the extent of the damage and is generally positive in many more cases of diphtheria than the clinical findings indicate When A V heart block or bundle branch block are present in this disease the prognosis is most serious

Diphtheria toxin may severely damage other structures that contribute to the efficiency of cardiac action and this burden may be added to the myocardial injury For example paralysis of the vagus and splanchnic nerves may augment the tachycardia and add the element of peripheral circulatory failure to the picture

If the patient survives complete healing of the damage produced by the toxin of the diphtheria bacillus in all of these areas is the rule Chronic heart disease does not result from diphtheria Complete heart block if present does not persist and if this conduction defect is found in later life it cannot be viewed as the result of diphtheria in childhood

Early and adequate treatment by antitoxin is the best therapy for the heart in diphtheria In view of the type of damage that has been described a convalescent period of at least three weeks is essential When cardiac damage is extensive in the severe cases small injections of glucose are invaluable The additional measures are the same as are employed when cardiac involvement follows any infection

SCARLET FEVER

There is a great deal of difference of opinion regarding the production of an endocardial lesion by the streptococcus that has been shown to

stand in an etiologic relationship to scarlet fever The earlier cardiac signs may be associated with the effect of a soluble toxin but close inspection shows that these are all analogous to the change that occur when rheumatic fever follows an attack of acute tonsillitis Even articular manifestations may be associated with scarlatinal infection although these are milder are associated with less effusion and tend to involve smaller joints The valvular involvement that is described as scarlatinal is identical with rheumatic endocarditis Similar electrocardiographic alterations are produced Consequently the bulk of present day evidence points to the fact that scarlet fever is merely the activating agent The patient quite often has a rheumatic constitution and a positive family history

I observed a similar response following erysipelas involving the face and scalp in a child of seven Two weeks after the initial infection subsided leaving the boy as bald as an onion a typical attack of rheumatic fever with joint manifestations developed A mitral lesion was discovered a month later During the course of the intervening years the development of mitral stenosis has been followed The last examination 20 years after the attack of erysipelas showed mitral stenosis and mitral insufficiency with considerable cardiac enlargement

## INFLUENZA

Although many symptoms of a cardiovascular nature are frequently observed following influenza we cannot say that this disease causes any permanent damage A cardiac examination at the height of the disease will reveal the usual changes associated with any other febrile disorder with the exception perhaps of the relative bradycardia During the course of influenza other arrhythmias such as premature contractions and marked sinus irregularities are not infrequent The pathology in this disease is obscure However if structural alterations do occur as some observers claim they completely disappear following convalescence

The postinfluenzal symptoms are usually shortness of breath precordial distress palpitation weakness and exhaustion All appear on slight exertion and may be regarded in most instances as manifestations of neurocirculatory asthenia (page 410)

## PNEUMONIA

The pneumococcus infection does not in itself cause serious heart involvement unless the endocardium is attacked (page 185) or suppurative pericarditis develops following extension of the process from the lung (page 171) Pneumonia may prove to be a most serious complication in the presence of advanced heart disease The cardiac failure occurring late in the course of this disease usually shows a poor response to the usual measures Routine digitalization of all pneumonia cases is not recommended However the use of the drug in the presence of auricular flutter auricular fibrillation or congestive failure is indicated As a rule water

sugar salt and oxygen are the most useful remedies in the treatment of the circulatory collapse in pneumonia

### TUBERCULOSIS

The effect of tuberculosis on the heart may be considered from many angles The tubercle bacillus itself only rarely attacks the heart When it does the pericardium and myocardium are invaded by direct extension from a neighboring focus or as a part of a general miliary involvement In the course of the latter process the endocardium may be seen to contain small tubercles of the miliary type at autopsy They are never important clinically However the pericardial process may heal in some cases with the subsequent deposition of calcium and by its constriction produce grave interference with diastolic filling (page 182)

In some cases an active tuberculous infection may produce alterations in either rate or rhythm of the heart that will attract attention of the patient toward the cardiac mechanism (case 64) Neurocirculatory asthenia not uncommonly accompanies tuberculosis

Alterations in the lungs during the course of the disease may in some cases place a strain on the right side of the heart and the symptom of chronic cor pulmonale may be observed (page 426) In other instances a sudden pneumothorax may produce pain suggestive of coronary occlusion If the mediastinal structures are displaced in advanced phthisis by adhesions a variety of confusing cardiac signs appear

Tuberculosis of the lungs is not evidence against the diagnosis of organic heart disease However because of the bed rest usually prescribed for the tuberculous patient congestive failure seldom appears Pulmonary tuberculosis often complicates congenital stenosis of the pulmonary valve (page 346) as a result of inadequate circulation in the lungs Likewise in engorgement of the vessels of the lung that is seen in mitral stenosis, pulmonary tuberculosis is rare but has been observed

The treatment of active tuberculosis of the pericardium and the heart has been discussed elsewhere (page 175)

### FOCAL INFECTION

The concept that infection in the teeth tonsil sinuses gallbladder cervix or gastro-intestinal tract is responsible for a variety of diseases has gained headway in recent years Although we possess no entirely satisfactory criteria for determining the presence or absence of infection in many of these localities the teeth and tonsils seem to bear the brunt of the attack of the focal infection enthusiasts Consequently many unnecessary operations have been performed that are not without danger in patients who have heart disease Bacteria gain entrance into the blood stream at times following these procedures and in some cases a fatal endocarditis results (page 197)

All the diseases of unknown etiology that affect the heart have at one time or another been blamed on the tonsils Reimann and Havens[310] point

out that one third of all surgical operations performed in a group of nearly 40 000 cases were tonsillectomies The extraction of diseased tonsils prevents the recurrence of quinsy and acute tonsillitis and may decrease the frequency of attacks of acute rheumatic fever However we must remember that this procedure does not offer to all patients a guarantee against the occurrence of rheumatic infection and subsequent heart disease Many studies of groups of tonsillectomized children that have been made by Kaiser[1,8] and others[3] reveal no great decrease in the incidence of rheumatic heart disease following operation when compared to control groups In view of the number of tonsillectomies performed today if this were the solution of the problem of rheumatic infection the incidence of this disease by this time ought to show a decided decrease Such is not the case On the other hand tonsillectomy itself may be followed by a number of serious complications By no means the least important of these is a violent flare up of a smoldering rheumatic state

It is unfortunate that the wide acceptance of the attractive theory of focal infection has elevated it in the minds of many to the position of a proved fact I believe that the treatment of heart disease by the eradication of these foci should always be governed by the circumstances in each case For example pain tenderness swelling and lymph node involvement speak for the presence of infection in a tooth and its removal should be considered Roentgen films alone should not decide the issue for they are often unreliable in these cases Similarly only tonsils that show a persistent redness accompanied by injection of the anterior pillars painful swallowing enlarged regional lymph nodes and systemic evidence of infection should be considered diseased and their removal recommended I do not believe that either the size of the tonsils or the cheesy material expressed from their crypts should be accepted as adequate evidence for a mandatory tonsillectomy As a matter of fact the debris that we so often demonstrate in the tonsillar crypts is harmless When treatment is begun for the patient s condition as a whole the lymphoid tissue in the pharynx and throat that previously suggested the presence of infection may take on a quite different appearance Needless to say surgical treatment of all foci of infection should be delayed until a complete survey of the patient has been made Surgical attacks on accessible foci in cardiac cases should never be recommended unless the evidence in each case leaves little doubt as to the presence of infection Prophylactic tonsillectomies are not justified The same rule should apply with respect to the teeth It still remains to be proved that any primary disease of the heart is the direct result of infection in the teeth

# 15

# THE HEART IN PREGNANCY

In the management of the cardiac patient during pregnancy many situations are encountered that demand a thorough knowledge of the diagnosis and prognosis of heart disease Numerous questions are likewise asked by patients contemplating marriage that call for an appraisal of the circulatory status and an estimation of the probable effect of the additional burden of pregnancy Certain rules of practice may be adopted in applying our knowledge of heart disease to these special situations These may be better understood if the fundamental principles upon which they are based are first briefly discussed

## THE PROBLEM

During pregnancy the heart has more work to do This is not the result of any single factor but is brought about by the many physiologic alterations that take place as gestation advances To begin with the gain in weight accompanying pregnancy places an extra demand on the circulation Moreover since this gain is also a local one the postural alterations produced may have a tendency in some individuals to add an extra burden during the course of pregnancy Too much significance however should not be placed on this single factor of increased body weight as a cause of heart strain for Jensen has cited four cases from literature where improvement in the circulation took place at the time of fetal death and not following delivery [1]

Aside from the patient s increase in weight the continued advance in uterine size with its increasing vascularity is an additional factor that adds to the work of the heart From this standpoint as Burwell has pointed out [47] pregnancy increases the cardiac burden by the development of wide communicating channels in the uterine wall in the manner of an arteriovenous fistula

Successive pregnancies probably have no permanent effect on the vascular bed itself There is nothing to prove that a "toxin is produced to activate changes in this area or to produce even a temporary vasoconstrictor effect that may increase the cardiac load

With elevation of the basal metabolic rate extra work is placed on the heart in fact the operation of total thyroid ablation was planned to decrease the metabolism and improve the circulation by decreasing the cardiac load In pregnancy the thyroid gland enlarges and it is natural to suppose that an increase in the work of the heart takes place and accompanies the increase that is observed in the basal metabolic rate

Recent studies confirm the fact that the circulating blood volume is increased during pregnancy Although there is some difference in the figures obtained by the use of the various gas and dye methods the increase in some cases has been found to be as high as 40 per cent Consequently, again we have proof of an increase in the cardiac load

Clinical and laboratory studies indicate that the normal heart adequately meets these demands placed upon it during pregnancy A slight increase in the blood pressure particularly the diastolic balances the increased peripheral resistance the pulse rate quickens, and the minute volume increases while the circulation time remains unchanged

## EXAMINATION OF THE HEART

If we apply the ordinary methods of examination to the heart in pregnancy to detect what changes if any take place the result is interesting and will lead us into a great deal of speculation

**Change in Size of Heart** In the first place the medical pendulum seems to be unwilling to come to rest in regard to the question of the presence or absence of cardiac hypertrophy However much depends on our conception of the word hypertrophy The heart does increase in size but this is entirely within the limits that would be expected when viewed in the light of the increase in body weight The heart under the fluoroscope appears larger in fact the actual measurements are often increased It must be realized however that as pregnancy continues the heart is elevated and perhaps rotated by the high position of the diaphragm under which circumstance accurate determination of the cardiac size becomes difficult (Fig 152) The cardiac shape may in some patients be considerably altered by these changes and present the appearance of mitralization (page 37)



Fig 151 Alteration in cardiac position as pregnancy advances Dotted line indicates heart's position at third month The solid line shows position two weeks prior to term

**Change in Position of Heart** This shift in the position of the heart may be reflected in the change in the electrical axis of the electrocardiogram which must not be viewed as evidence in favor of hypertrophy In pregnancy there is a tendency for an inversion of the P wave and T wave to occur in the third lead and Pardee has called attention to a deep Q-wave in the same lead that may accompany a normal pregnancy (Fig 153) All these changes in the electrocardiogram may be explained on the basis of the change in cardiac position

**Appearance of Murmurs** The most common finding in the obstetrical department that causes the patient to be referred for cardiac study is the presence of a murmur Since this physical sign continues to be so intimately linked with heart disease in the minds of most physicians furthe

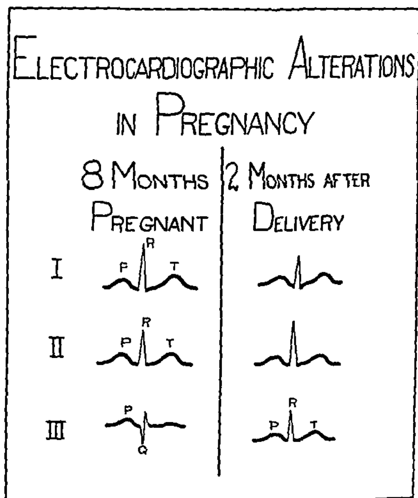



FIG 153 The electrocardiogram in pregnancy

special study of these patients is requested During pregnancy a systolic murmur over the pulmonary area should cause no alarm It is produced in many instances by the shift in cardiac position that is due to the steady elevation of the diaphragm It is usually louder in recumbency and may almost disappear when the patient is in the erect position This pulmonary systolic murmur appears after the fourth month of pregnancy At times these functional systolic murmurs may be heard over the whole pre

cordium but they are usually loudest in the second interspace to the left of the sternum Functional diastolic murmurs have been described but I have not heard them The pulmonic second sound may be accentuated during pregnancy because of the change in cardiac position that serves to advance the valve nearer the chest wall where its sound is more clearly heard Before a diagnosis of heart disease is made during pregnancy these physiologic alterations should be kept in mind Examination of the heart during pregnancy is not easy since enlargement of the breasts makes percussion and auscultation more difficult

**Other Diagnostic Signs and Symptoms** To confuse the picture further other reliable diagnostic signs and symptoms are of less value during pregnancy for example edema and dyspnea

It is not at all uncommon for edema of the feet to occur in normal women toward the end of pregnancy because of pressure on the pelvic veins and alterations in the capillary bed of the extremities

Likewise when dyspnea is complained of allowance must be made for the high position of the diaphragm that crowds the lungs and for the other anatomic and physiologic alterations just described In the cardiac examination during pregnancy reliance must be placed on diastolic murmurs either apical (mitral stenosis) or basal (aortic regurgitation) harsh apical systolic murmurs in patients with positive rheumatic histories engorgement of the neck veins enlargement and tenderness of the liver thrills unmistakable displacement of the apex beat or widening of the heart at the base serious arrhythmias like auricular fibrillation auricular flutter pulsus alternans or heart block friction sounds and the signs of chronic hypertension or nephritis

**Etiology** The majority (80 per cent of our series) of patients of child bearing age who have heart disease suffer from the rheumatic type with mitral stenosis Active rheumatic disease however is rare during pregnancy Congenital defects are present in a very small percentage of the cases whereas hypertension nephritis syphilis and arteriosclerosis can be grouped together as infrequent causes of cardiac complications (Table IX)

TABLE IX

TYPES OF HEART DISEASE

| | NUMBER | PERCENTAGE |
|---|---|---|
| Rheumatic | 32 | 80 |
| Congenital | 2 | 5 |
| Hypertensive | 2 | 5 |
| Miscellaneous | 4 | 10 |

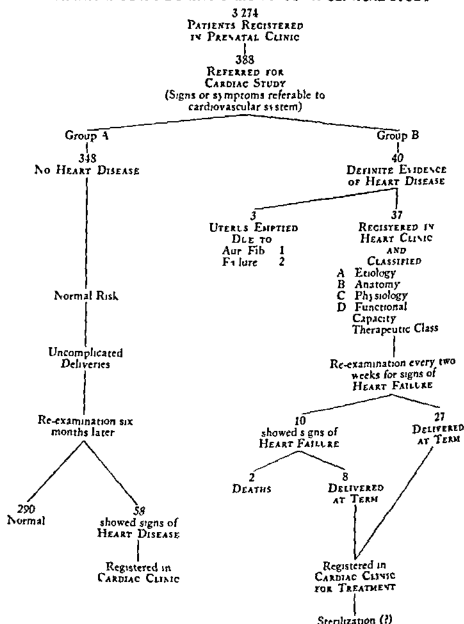
## CLASSIFICATION

For purposes of diagnosis and treatment a working classification of the patients presenting signs or symptoms of heart disease during pregnancy is essential Prenatal patients referred to the Cardiac Clinic of the Woman's

College Hospital after the first examination are divided into Groups A and B (Table X)

TABLE X

HEART DISEASE DURING PREGNANCY—A CLINICAL STUDY




**Group A** Patients who have systolic murmurs questionable degrees of edema, palpitation or dyspnea together with a negative rheumatic history

and no abnormal alterations in cardiac size or contour are placed in Group A The presence of heart disease cannot be proved and these patients (we assure the obstetricians) are excellent risks We tell the patients that they have normal hearts as far as we are able to estimate during pregnancy They are urged however to return for one examination following delivery

**In Group B** are placed all the patients who have cardiac enlargement diastolic murmurs and any of the signs of organic heart disease above mentioned We separate the patients belonging to this group and focus our attention on them for they are the ones most likely to develop cardiac complications as pregnancy advances We do not include in Group B any of the cases of mitral regurgitation and for purposes of this study we have allowed a large number of these patients to remain in Group A Group B is subdivided according to the classification of the American Heart Association (page 59) We consider this system most useful inasmuch as the obstetrical risk is in large part governed by the presence or absence of manifestations of congestive failure Likewise placing the patient in one or the other of these groups after the study is completed is a matter of great convenience It helps to establish proper treatment at an early date but it does not necessarily mean that the patient will remain permanently in the group nor does it indicate that the management will be group management and not adapted to suit the needs of the individual patient Seventy five per cent of our Group B patients belong in Class I 20 per cent in Class II 3 per cent in Class III and 2 per cent in Class IV

## MANAGEMENT

Patients in Group A do not of course require any special care as far as the heart is concerned

In Group B the patients in Class I and many in Class II if carefully watched can usually be counted upon to come through pregnancy and delivery without complications They report to the Cardiac Clinic once a month until the sixth month and are then seen at intervals of two weeks until they enter the hospital for delivery

**Rest** should be prescribed for Group B patients to reduce the demand made upon the heart to a degree consistent with the estimated reserve In the absence of any signs of congestive heart failure however an excessive amount of rest is detrimental to the patient Exercise of mild degree in the open air assists venous return to the heart and is decidedly beneficial

**General Measures** Group B patients are advised to avoid upper respiratory infections as much as possible As pregnancy progresses the household duties are lightened in each case to allow the patient to keep within the limits of her cardiac reserve This is estimated at each follow up visit when the progress notes are recorded and the examination of the patient is completed

**The laboratory procedures** indicated in cases where cardiac disease

is complicated by pregnancy include urinalysis Wassermann electrocardiogram and orthodiagram When these are obtained and evaluated the patient can be properly classified and her program outlined

**Follow up visits** give opportunity to check for errors in classification caused either by a mistake in interpretation of the findings or by a change in the patient s status as pregnancy advances On these occasions the blood pressure the respiratory rate pulse rate, and body weight should be recorded The feet should be inspected for signs of edema and the lung bases carefully examined If rales persist in the lung bases bed rest for two or three days followed by re examination should be the routine prescription The electrocardiograms usually do not have to be repeated unless arrhythmias are present that elude clinical detection

## Delivery

All Group B patients are admitted to the hospital two weeks before term for rest and additional observation Pregnancy is allowed to terminate normally Most of Class I and many of Class II patients deliver spontaneously with little trouble although the second stage of labor is often shortened, when indicated by the application of forceps Ether anesthesia can be used safely for the whole group The longer convalescent period allowed in the hospital usually means that the majority of these patients are discharged in excellent condition Unless an earlier date is indicated for some special reason they return in six weeks to the Cardiac Clinic for the first follow up study

Patients in Classes III and IV require close attention The prognosis of Class III patients is guarded while those in Class IV usually have a poor prognosis The complication that causes most concern to internist and obstetrician who work together in these cases in Classes III and IV is congestive failure It is responsible for 74 per cent of fatalities according to the recent report of Carr and Hamilton [5] Pneumonia pulmonary infarction sepsis and embolism are more frequent complications in these patients because of the influence of the congestive failure

**When congestive failure** appears it is usually during pregnancy and rarely during labor when the strain is supposed to be the greatest The reason may be better understood when we consider the fact that the patient is in labor a short time compared to the long period of pregnancy Nevertheless the influence of a poorly conducted labor in precipitating congestive failure must never be underestimated An upper respiratory or other infection may often play a large part in imposing the *additional* burden that upsets the patient The earlier in pregnancy congestive failure appears, the poorer will be the prognosis More frequent prenatal visits of the cardiac patient to her physician are mainly for the purpose of detecting the signs of failure as early as possible If during pregnancy a patient is seen presenting signs of advanced decompensation some one has usually fallen down on the job

The early recognition of congestive failure in pregnancy is not easy

but is possible if careful examinations are carried out The symptoms of dyspnea and palpitation together with the signs of tachycardia and edema must all be evaluated in the light of the physical state On the other hand congested neck veins orthopnea gallop rhythm pulmonary edema pulsus alternans are all advanced signs of failure Sudden paroxysmal dyspnea is rare as a complication of rheumatic heart disease but can occur in the presence of pulmonary overloading produced by a strong overactive right ventricle The initial attack occurred during labor in one patient of our series who suffered from hypertensive cardiovascular disease Although this patient was successfully delivered death occurred during another seizure two months after discharge

At times in doubtful cases estimation of the venous pressure is a very great help in the early diagnosis of congestive failure (page 54) However congestion of the lungs should be suspected when persisting rales are heard at the bases at any routine visit during pregnancy Rales should always be regarded as a warning of approaching danger and bed rest and digitalis prescribed The speed of digitalization is always determined by the condition of the patient When improvement takes place the drug should be continued in maintenance dosage until the time of delivery Pregnancy offers no contraindication to the use of the usual diuretics including the mercurial group

The extent of the bed rest will depend on the response shown to the treatment If improvement is rapid the patient may be allowed to be about again at an early date Some patients however may have to remain at nearly total bed rest until delivered At term the patient who can undertake but little exertion without great discomfort is in no condition to stand labor and should not be allowed to deliver spontaneously

If the patient when first seen is in severe congestive failure medical treatment should be given a thorough trial since the first aim of the physician should always be to restore cardiac balance Attention is then directed toward the termination of the pregnancy if there has been no adequate response to the measures employed However let me hasten to add that medical treatment seldom fails to restore enough circulatory balance to make subsequent intervention a much less dangerous measure Haste in these situations only increases the maternal mortality rate

If auricular fibrillation is present as Mackenzie originally stated [1] the prognosis should be considered more serious However the management remains the same The attempt should be made to control the ventricular rate by full doses of digitalis and if the usual satisfactory result is obtained operative interference can be delayed until a rest period improves the risk

The additional measures to be considered in the treatment of the decompensated patient during pregnancy differ very little from those already outlined Dietary regulation (page 548) has for its guiding principle the administration of suitable amounts of glucose In cases where the heart failure is attended by considerable cyanosis oxygen if available will be of

great benefit since it also increases the chances of survival of the baby (page 98) A flow of four liters per minute using the nasal-catheter apparatus is satisfactory in emergencies Higher concentrations of oxygen should be used with great care in these patients since nearly all of them suffer from advanced mitral stenosis The danger of a higher percentage lies in producing bronchial irritation cough and pulmonary edema

**Termination of Pregnancy** Many facts are to be carefully considered before choosing the method to be used in terminating pregnancy Each case must be decided on its own merits for in this matter no set of rules can be laid down and dogmatically followed A great deal depends upon the time the patient is first seen If very early in pregnancy and congestive failure is already present the outlook is serious and therapeutic abortion is the method of choice after careful preparation of the patient In further advanced borderline cases the history of previous pregnancies may serve as a guide to the procedure However, if in doubt concerning the method of choice it is always best to do nothing, since patients with congestive failure who are subjected to the additional shock of ill timed interference invariably do poorly Therapeutic abortion should never be performed until congestive manifestations clear If labor begins spontaneously to further complicate the situation morphine should be given in an attempt to postpone delivery until circulatory balance has been restored

**Cesarean Section** In Class III and Class IV patients the operation of cesarian section has much to recommend it It can be carried out under spinal or local anesthesia depending on the preference of the surgeon and in well prepared patients can be accomplished in a very short time with but little additional strain on the circulation Of course the dangers of hemorrhage shock anesthesia and embolism are added to a poor risk but I believe that these are more than overbalanced by the strain of a long labor

**Sterilization** can be carried out at the time of operation if cesarean section is the method of choice Sterilization has much to recommend it and should always be done if the heart condition is too severe to stand the strain of a normal delivery (Class III and IV patients) and when the patient with heart disease already has more children at home than her fast diminishing cardiac reserve will permit her to care for efficiently Here again the factors present in each case will guide the selection of the proper procedure

**Anesthetic** There is little to fear from the anesthetic if it is wisely chosen and properly administered Ether by the open drop method is safe in the majority of cases Chloroform adds a risk that is not negligible Nitrous oxide and oxygen mixture may be used if skillfully given while ethylene has furnished good results in clinics that are properly equipped for its use As a general rule anesthetics administered by mouth or injection are not as satisfactory as the ones administered by inhalation Once injected the action is harder to control, and in some cases postoperative complications occur No matter how trivial the operative procedure or how good the risk appears to be cardiac cases at all times require careful

handling Consequently psychic shocks worry insomnia are all indications to postpone operations until the patient is in better condition Neglect of this last principle may occasionally be followed by disaster

The use of pituitrin to speed labor in cardiac patients is to be condemned for in the conduct of labor in the presence of advanced heart disease speed is not as essential as the conservation of the patient s energy Observation of the blood pressure respiratory rate and heart rate should be made frequently during labor The neck veins and the patient s color should be watched closely Increase in the heart rate congestion in the neck veins and rales in the chest are danger signals Many cardiac patients are unable to stand the recumbent position and should be delivered with the back of the table elevated to about 30 degrees The Trendelenberg position should never be used

Usually if cardiac failure is avoided by the combined efforts of cardiologist and obstetrician during pregnancy it does not appear during labor or the puerperium *If it does appear after delivery some other precipitating cause* must be suspected and searched for Sepsis infarction phlebitis and mastitis are a few of the more common causes to be kept in mind

### Puerperium

The patient must not be neglected during the puerperium since following the marked fall in the intra abdominal pressure and the consequent shift in the cardiac axis circulatory accidents may be occasionally encountered Sand bags on the abdomen are recommended by some obstetricians to *maintain pressure* and lessen the shock of sudden circulatory readjustments

## SHOULD PREGNANCY BE CONTEMPLATED BY THE CARDIAC PATIENT?

This question is difficult to answer offhand but may be satisfactorily worked out for each individual case when all the facts are carefully set down *The type of heart disease present and its severity should first be considered* If advanced rheumatic heart disease is discovered and the cardiac reserve is low or if the patient has already survived one or more attacks of congestive failure the decision must be in the negative In established but less advanced cases the decision may be more difficult If the patient has had rheumatic heart disease for some time and has been under the constant supervision of the family physician no one is better suited to give this opinion Previous entries on the office card give valuable clues to the degree of progress of the patient s cardiac lesion and are most useful If the decision is still difficult it is best to make a mistake on the safe side than to be too optimistic Generally it is satisfactory to place the facts squarely before the patient and her husband and outline the risks that must be assumed The station in life and the economic condition of the

family in question are points to be weighed in the balance In other word will the patient be in a position to take good care of herself during the pregnancy Unfortunately for each patient who seeks this advice before marriage the physician will have many who come in for advice when pregnancy is already present

Opinions governing subsequent pregnancies cannot be entirely based upon observations made during the initial one The cardiac lesion since it is usually of the rheumatic type may be progressing in which event the reserve diminishes Many times it is difficult to say whether this is the effect of the first pregnancy on the heart or whether it is the result of an advancing rheumatic infection If some years have gone by since the first pregnancy the age of the patient must be given due consideration, since older patients with the same degree of damage do not do as well as the younger ones Finally it may be stated as a general rule that if the heart lesion is trivial the patient may have two or at the most three children If on the other hand the lesion shows signs of progressing and particularly if the patient is over 30 she should realize that the second pregnancy may not be as smooth as the initial one and that the risk assumed is far greater She will then usually be content with one child I must admit that I have seen many instances where a second pregnancy was successfully weathered in spite of advanced rheumatic heart disease when the patient had been warned against it

Gilchrist[11] studied 109 cases of fatal cardiac rheumatism in order to discover the effect of repeated pregnancies on the course of the disease A comparison was made with males nulliparae and parous women regarding the average age of death mode of dying duration of the cardiac disease and the rate of progression to fatal termination No significant difference was found in the duration of the disease in nulliparous and parous women Auricular fibrillation Gilchrist found is not necessarily an indication of an additional burden placed on the heart during the child bearing period Its incidence he believes is largely determined by the length of survival from the time of the first involvement of the heart Women dying from congestive heart failure (the mode of death in 92 per cent of the whole group) had families averaging 4 5 children each a fact that supports the contention that the strain of frequent child bearing brings earlier death Gilchrist concludes that one or perhaps two pregnancies have little effect on the course of the disease in the majority of the cases but repeated pregnancies will definitely shorten the *life span* of women suffering from rheumatic heart disease since they increase the incidence of congestive cardiac failure

## SUMMARY

## The Heart in Pregnancy

### I THE RISK

1 All patients in Group A (Table X) do well If carefully managed those in Group B (Classes I and II) give little trouble

2 In patients who have established mitral lesions (usually stenosis) with little or no cardiac enlargement the risk is slight
3 As a rule the risk is directly proportional to the size of the heart There fore routine fluoroscopic examinations should be made during pregnancy on all patients who have established cardiac lesions
4 The most important single factor in the determination of the risk is the cardiac reserve This can be estimated by inquiry concerning patients ability to perform ordinary household duties without discomfort Valve lesions *per se* have little influence on the risk
5 Danger signals Signs of failure appearing at any examination auricular fibrillation or great increase in cardiac size (Apex beat or left border in axilla) and a previous history of congestive cardiac failure
6 Good prenatal care and co operation of patient will greatly improve the risk in many cases and permit delivery of a normal child at term

II RULES FOR MANAGEMENT

1 If cardiac lesion slight one or two pregnancies permitted If cardiac lesion moderate one pregnancy permitted Pregnancy should be for bidden in cases showing
   (a) Previous history of heart failure
   (b) In presence of an advanced lesion with auricular fibrillation
2 When patient who presents contraindications to pregnancy is seen during the first three months empty the uterus If seen later treat congestive failure (bed rest and other measures) then do cesarean section OPERATIVE INTERFERENCE IS CONTRAINDICATED IN THE PRESENCE OF CONGESTIVE FAILURE!
3 The patient should be examined frequently during the later months of pregnancy IT IS EASIER TO PREVENT CONGESTIVE FAILURE THAN IT IS TO TREAT IT!
4 For delivery or operative interference inhalation type of anesthetic is preferable ether ethylene alone or combined with local
5 When pregnancy is complicated by a cardiac lesion the best results are obtained when pregnancy is allowed to follow a normal course The second stage of labor may be shortened by forceps
6 Induction may be a more serious trial than normal labor at term Acute left ventricular failure followed attempted induction in one case in our series

# 16

# ALLERGY AND THE HEART

By RICHARD A KERN, M D *

There is as yet no proof that the heart itself can be the site of an allergic reaction That is to say no one has demonstrated in the heart after exposure to an allergen the occurrence of edema or of smooth muscle spasm the basic phenomena of the allergic response There is, however good clinical evidence that an allergic reaction may be the trigger mechanism which may precipitate certain symptoms referable to the heart notably some of the cases of paroxysmal auricular tachycardia A similar relationship has been suggested between an allergic reaction and other cardiac diseases but the evidence is far from convincing Of major importance from the view point of clinical medicine is the very serious role which allergic disease especially of the respiratory tract so often plays in patients who are suffering from some form of cardiac disorder

## CARDIAC CONDITIONS PROVOKED BY AN ALLERGIC MECHANISM

It is an axiom that the purely allergic reaction is wholly reversible An urticarial wheal disappears without leaving behind it any trace of structural change The nasal mucosa which for weeks has been the site of marked *edema during the hay fever season reverts to normal within a few hours* of the removal of the offending pollen from the inspired air The smooth muscle of gut or bronchial tree even after many episodes of allergic spasm shows at most a very trifling and usually no hypertrophy

If this reversibility of an allergic reaction be as true of a possible cardiac allergy as it is of allergic manifestations in other organs and tissues then in the intervals between allergic attacks the heart should be normal according to every criterion of examination Furthermore it should be possible to elicit the allergic response on adequate exposure to that to which the person is sensitive and he should remain free of symptoms so long as such exposure is avoided

These conditions are rarely fulfilled in patients known to be allergic and who have symptoms of cardiac disease As a rule such patients give some evidence of structural or functional cardiac abnormality throughout the interval between allergic episodes At this point the question might be raised Will not a permanent structural change result at times from frequent repetition or prolonged duration of an allergic response as for

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example nasal mucous polyps in perennial allergic rhinitis? True but before that final stage of polyposis is reached there has been a long period without permanent structural change simply an edema which promptly subsides when there is no longer any exposure to the allergen which provoked it Only rarely, even during the beginnings of symptoms does one encounter in the intervals between allegedly allergic cardiac episodes a heart that is altogether normal in structure and function As a rule one gets the impression that the allergic reaction is an added factor which provokes symptoms in a heart that has already been damaged by some other disease process

Even when the heart appears to be normal between attacks one is not justified in concluding when cardiac symptoms are produced on exposure to a substance to which the patient is sensitive that the heart itself is the site of the allergic reaction The reaction might have occurred elsewhere and might have affected the heart indirectly by way of nerve pathways This will be discussed further under paroxysmal auricular tachycardia

This discussion may seem unduly theoretical for a clinical text but it has this fundamental significance If the cardiac condition were due only to allergy then its management would call for treatment primarily and perhaps solely along allergic lines But if as is the rule one is dealing not only with allergy but with a heart that is the site of some additional pathologic process then allergic therapy is only an incident in the management of the underlying cardiac disease

## PAROXYSMAL AURICULAR TACHYCARDIA

This is perhaps the outstanding cardiac disorder in which an allergic mechanism may play a part The systematic description of paroxysmal auricular tachycardia its etiology diagnosis and treatment will be found in Chapter 12 (page 382) the present discussion is limited to the allergic aspects

In a series of 28 cases of paroxysmal tachycardia seen by me eight gave sufficient evidence of food allergy to warrant the conclusion that the allergy played a major role in the production of the arrhythmia Criep (personal communication) has had a similar experience L P Gay[11] has also encountered cases of this type The following patient reported by me in 1932[18] well illustrates the salient points

## ILLUSTRATIVE CASES

**Case 91** Miss E S a nurse aged 40 years was seen by me on December 9 1931 in the midst of an attack of tachycardia She had been subject to such attacks as long as she can remember at least since the age of five They have been characterized by sudden onset of rapid heart action usually in relation to indigestion The indigestion was usually caused by eating nuts which always upset her The attacks stop in a few minutes as suddenly as they start usually after the use of one or another maneuver upon which experience has taught her to rely The most effective of these has been to stand

leaning forward with knees straight and finger tips touching the floor The present attack had begun the preceding evening while attending a dinner dance at which she had eaten freely of nuts Being loath to try the above described stunt on the dance floor she waited until she got home only to find that it would not work When I saw her at one o clock the next morning the attack had lasted four hours the pulse being 180 I prescribed capsules of quinidine sulfate 0 Gm one to be taken every four hours The first dose produced some nausea and itching The second was followed by similar but more severe symptoms and a crop of hives The heart rate dropped suddenly to normal within an hour after the second dose

When seen on January 1 193 73 days after the attack she was normal in every respect There were no discoverable abnormalities in heart or circulation and her circulatory response to exercise was excellent She had always been much given to athletics including swimming golf and riding and has never experienced any cardiac limitations in these activities An electrocardiogram on this date showed a normal tracing

The following significant facts and data were subsequently established all her life she had been subject to hives Her mother had typical and severe migraine Skin tests showed her to be skin sensitive to some and not to others of the foods which could provoke attacks of tachycardia Avoidance of these foods was followed by comparative freedom from attacks for a number of years

On January 5 1940 after a banquet at which she ate not wisely but too well she developed another severe attack of tachycardia The second dose of 0 1 Gm of quinidine sulfate stopped the attack which had then lasted nearly ten hours The smaller dose of quinidine produced nausea and some itching but no hives

Discussion This case illustrates several points which are highly important in clinical problems involving the proof of an allergic factor in the production of a specific disease picture

1 The Patient Is Allergic For years she has experienced attacks of an obviously allergic condition hives She is probably of allergic heredity her mother having had typical migraine, which is commonly of allergic etiology An allergic individual is one who is born with the characteristic *of becoming sensitized to things in his environment more easily than do* normal persons This characteristic of easy sensitizability may manifest itself at any time during the patient s whole life time and in a wide range of tissues and organs

2 In an Allergic Patient Therefore Allergy Must Be Routinely Suspected as a Possible Etiologic Agent in Many Illnesses for example paroxysmal auricular tachycardia in this patient

3 The Clinical Test Gives the Necessary Proof of an Allergic Etiology When she avoids those things to which she is sensitive, she is symptom free When she eats the offending foods she develops attacks of tachycardia

4 The Patient Is Sensitive to Quinidine Drug idiosyncrasy occurs far more frequently among those who are obviously allergic The drugs to which patients are most commonly sensitive are aspirin quinine and the iodides Those sensitive to quinine are usually sensitive to its derivative quinidine If one third of cases with paroxysmal auricular tachycardia are associated with allergy then the chances of encountering such clinical idiosyncrasy are not to be overlooked All prospective candidates for quinidine therapy should be questioned as to a possible quinine idiosyncrasy In case of such idiosyncrasy great caution and a sharply reduced dosage

are called for In this same connection attention is called to the fact that acetyl beta methyl-choline and related substances which have proved effective in arresting paroxysms of tachycardia may at times precipitate an attack of asthma in those inclined to that disease They should therefore be used with caution in all allergics and preferably not at all in those who are obviously asthmatic (see Case 71)

5 After Countless Paroxysms of Tachycardia During More Than 40 Years Her Heart Continues to Be Normal The manifestations of allergy are primarily functional and reversible Except under extraneous unfavorable circumstances (e g infection in allergy of the respiratory tract) they do not lead to organic change At this point the question could be asked might this not be an instance in which the allergic reaction actually takes place in the heart itself? Perhaps But the facts do not warrant the conclusion, since the same effect might have resulted through a reflex pathway from an allergic reaction elsewhere in the body The following case reported by me in 1926[190] illustrates the point

**Case 92** A woman of 35 years of age ith no previous h story of card ac d sease and no evidence of subsequent development of such d sease in the e ght years thereafter was subjected to the Rubin test for patency of the fallopian tubes by the intra uterine inject on of a r A few minutes after leaving the gynecolog st s office she experienced sharp pa n in the left upper abdomen with radiation to the neck At the same time there de eloped a paroxysm of tachycard a

She returned to the gynecologist s office where I sa the patient with him The present ing featu es were the complaint of pain and a heart rate of 15? per minute Reasoning that both pa n and tachycard a were caused by a bubble of air under the left half of the diaphragm we placed the patient flat on the table and elevated the foot end Not only d d the pain promptly stop but the h art rate fell in a few seconds to 76 Some minutes later when the patient assumed the e ect po ition both pain and tachycardia returned to be promptly rel eved when she was aga n inverted Some hours later when the air bubble had been absorbed she was free of symptoms

Eighteen months later she ent through her first pregnancy without trouble and was well when I st heard from n 1934

Obviously the paroxysm of tachycardia must have been mediated by a reflex mechanism

When an attack of paroxysmal tachycardia lasts long enough even though it was initiated by an allergic mechanism and in the absence of obvious cardiac disease then the exhaustion of even a normal heart might result from the prolonged excessive effort When a patient is seen for the first time in the latter stage the physician may well assume the presence of serious myocardial damage and may even overlook the paroxysmal and functional nature of the underlying tachycardia The next case illustrates this point

**Case 93** In December 19 6 I was called to see Mrs M V age 6 in consultation with her family phys cian For some years she had had h art trouble with increas ng breathlessness and palpitation on exert on so that her activ ties were more and more lim t d S x we ks before my v s t she had been forced to tak to her bed because of dyspn and ncreas ng per pheral ed ma Her doctor believed her to be in extremis from circulatory fail re probably based on an arteriosclerotic myocarditis The appearance of

the patient fully justified this view orthopnea cyanosis many rales at the lung bases a swollen liver considerable dependent edema The heart rate was about 200 The administration of digitalis over a period of the last two months had been of no avail

There was one item in the history however which in my opinion had not been given adequate consideration The earliest evidences of heart involvement were attacks of palpitation and tachycardia that had been occurring for at least 0 years, and long before breathlessness or any other sign of circulatory inefficiency appeared Moreover these attacks of tachycardia came on suddenly independent of exertion and they stopped as suddenly as they began A diagnosis of paroxysmal tachycardia was therefore ventured and quinidine treatment was begun at once

On the second day the heart rate fell suddenly to under 100 and the improvement in the clinical picture that followed was most striking For a time short paroxysms recurred several times a day but grew less frequent as a suitable daily ration of quinidine was reached On December 30 19 6 she was able to make a 175 mile motor trip to the home of friends in Philadelphia The next day an electrocardiographic study in the midst of an attack was made The cardiac rate in the upright position was 195 and in the recumbent position 185 The rhythm was regular On the next day January 1 1937 the tracing showed a normal rate of 5 and a regular rhythm Dr Wolferth reported 'The tracings show beyond question that the tachycardia is of paroxysmal auricular form The negative T waves would point also to definite myocardial disease The patient soon learned to adjust her quinidine dosage to prevent more than an occasional short attack of tachycardia

Over four years later on April 17 1931 the patient having been fairly well in the interval another electrocardiogram was made It showed normal T waves At the time of writing (February 1940) the patient continues to be remarkably well in spite of her 80 years

**Discussion** This patient had had asthma in childhood ragweed hay fever every autumn for many years a rash each time she ate strawberries and digestive upsets whenever she ate certain foods Several members of her family had been asthmatic The avoidance of the foods causing indigestion also greatly reduced the frequency of the paroxysms of tachycardia so that she has gone as long as six months without an attack and without taking quinidine

## OTHER CONDITIONS

From here on it becomes difficult to enumerate additional cardiac conditions provoked by an allergic mechanism In most of those to be mentioned in this section the allergic mechanism has been suggested by some enthusiastic allergist but his view has not received confirmation The usual fallacy in the allergist s conclusion has been the assumption that because a cardiac symptom or disease became worse at the time of an allergic episode that allergy was directly responsible for such exacerbation The truth is that any sufficient overload allergic or otherwise can bring on symptoms in a diseased heart it is the overload that is responsible not the nature of the overload In a few instances an exceptional case of a condition may be on an allergic basis whereas the overwhelming majority have no such connection The double danger then is that the allergist assuming too much on the basis of his few cases makes unwarranted generalizations about the role of allergy in that condition while

the clinician who is not sufficiently allergy minded completely misses the occasional case caused by allergy occasional yet one in which treatment offers so much more than in most other kinds of heart disease

What follows is therefore an attempt both to curb the allergist's unwar ranted enthusiasm, as well as to put the general practitioner on his guard for the occasionally allergic condition

### Paroxysmal Auricular Fibrillation

Not to be confused with ordinary auricular fibrillation this much rarer form of the arrhythmia has been attributed to various factors including toxic states (acute infections, anesthesia thyrotoxicosis poisoning by car bon monoxide, alcohol tobacco etc ) gastro-intestinal disorders or even emotional upsets (page 394) A significant fact from the standpoint of a possible allergic mechanism is that the paroxysmal arrhythmia is at times the only abnormal cardiac finding

## ILLUSTRATIVE CASE

The following case is to my knowledge the first recorded instance of an allergic paroxysmal auricular fibrillation

**Case 94** Mrs A W white aged 61 has experienced characteristic attacks of palpita tion for at least 5 years and probably longer The attacks u ed to come at intervals of weeks or months beginni g sudd nly last ng a matter of m nutes and stopping rather more slowly than they began She fi st consulted Dr Leaman n 1930 but never presented herself during an attack An electrocardiogram in an interval showed a normal tracing In 1933 she survived an att ck of Type 3 lobar pneumonia in the midst of which she had a paroxysm of fibrillat on that was promptly controlled by quinidine Following th sudden death of her nothe from coronary occlus on and the prolonged illness of her husband the patient experienced more f equent attacks that lasted up to several hours In one of th se D Leaman secured an el ctrocardiogram that showed auricular fibrilla tion yet in the subs quent nterval he found a normal traci g (Fig 144) During 1937 she had attacks at ntervals of days or weeks but was able to control them promptly with quin dine Some of th se paroxysms followed oon after a meal In September 1937 she was admitted to a hospital for study but all examinations including Roentgen investi gation of g llbladder and gastro nt stinal tract gave negative findings

In January 1938 Dr Leaman refe red her to me for investigation of a possible sens tivity From the standpoint of allergy these points were highly s gnificant as a ch ld she had eczema and even re ently she has had an tchy scaly rash back of an ear For many ye s she had typical and rather evere m graine A paternal uncle and her p ternal grandmoth r h d eczema and a paternal uncle had migraine A maternal uncle had hay fev r Sk n tests show d the patie it to be sens tive to a number of food

In the two year nce h wa tested she has experienced far fewer and milder attacks and th se have u ually follo d a break in her diet

### Extrasystoles

Rowe[32] Wirley[416] and others have reported the occurrence of extra systoles in allergic patients after the eating of certain foods and their disappearance after avoidance of the specific excitant Here again although an allergic mechanism might be involved it seems more likely that the arrhythmia is provoked in other ways (vagus reflex toxic action etc )

cardiac condition are overlooked In others there is no mistaking the presence of both diseases Then there are those in whom the cardiac failure so dominates the picture that the co-existing asthma is not recognized

Asthma is a peculiarly serious complication for a patient with heart trouble for reasons too obvious to mention The recognition of the asthma in the cardiac patient is peculiarly important because the treatment of the asthma offers so much in the way of probable help not only for the asthma but indirectly for the heart by reducing its load Here then is a subject that should challenge the interest of every doctor who treats patients with heart disease

## Does Asthma Cause Heart Disease?

This question has given rise to more discussion among allergists than might be anticipated at first glance The answer to the question *probably* depends on a number of circumstances

Asthmatic symptoms occur in one of three ways (1) Short, clear-cut paroxysms lasting minutes or hours and with symptom free intervals whose length is determined by the time elapsing between intermittent contacts with an external cause (2) Continuous wheezing for weeks months or years often mild at times severe and usually with slight to severe paroxysmal exacerbations Continuous asthma may be caused by constant exposure to external causes or to a continuation of external causes and internal causes, notably infection with or without bacterial allergy (3) Status asthmaticus denotes an intensely severe and prolonged attack of dyspnea lasting days or even several weeks often with fever, usually with scanty viscid bronchial secretion that is hard to cough up and may produce bronchial obstruction atelectasis and even fatal asphyxia

**How Can Asthma Affect the Heart?** There is some experimental evidence that in the perfused heart of a sensitive animal there results a diminished coronary flow Criep[75] has shown that in man during an asthmatic paroxysm there are transient electrocardiographic changes that might be a result of such a reduction of blood supply This might lead to symptoms such as premature beats or possibly even angina Such paroxysmal asthma of itself, however, apparently does little or no permanent damage to the heart

Continuous asthma by reason both of its incessant annoyance and increased and continued exertion is undoubtedly an important factor in aiding and abetting other causes of heart disease of whatever nature they may be It probably is also responsible for some heart disease in that its most serious complication emphysema may lead to eventual myocardial trouble and failure (page 427) As yet there are not available a sufficient number of cases observed over many years to draw any statistical conclusions although Old [83] and Dublin and Marks[83] on the basis of life insurance data find a death rate among asthmatics that is 21 to 30 per cent higher than the normal This increased death rate is largely attributed by them to cardiac disease

Emphysema In regard to the development of serious emphysema in the course of asthma I would like to record two clinical impressions and one note of diagnostic caution One important factor in the etiology of emphysema in asthma appears to be an inherent quality of the pulmonary tissue the grade of the rubber" as Osler expressed it Of two asthmatic patients whose diseases appear to be identical the one may go for many years without developing emphysema whereas the other s lungs reach an advanced degree of emphysema in a year or so A second point that seems to be important in regard to the development of emphysema is that the shape of some chests is such that their owners have a shorter way to go than do others before their bony thorax has reached its limits of expansion It certainly seems to me that the asthmatic who begins with a thick stocky chest with ribs that approach nearer to the horizontal and with a deep antero-posterior diameter, makes poorer weather of his asthma than does the asthmatic whose chest at the start is rather longer with sloping ribs a cross section that is more oval than round and consequently showing wider variations in chest capacity at the extremes of the respiratory cycle

The diagnostic caution is this a diagnosis of emphysema should be made only with great hesitancy during the presence of frank asthmatic symptoms The roentgenologist is particularly prone to make this error when reading the films of an asthmatic patient yet films made a few minutes after the asthma has been relieved by epinephrine will be reported as normal A comparison of physical findings before and after epinephrine is always in order in such cases Vital capacity figures are then particularly helpful

### Diagnostic Problems

Many cases of co existence of asthma and heart disease in the same patient present no difficulties in this regard Pronounced asthma is easily recognized by the experienced clinician and the same may be said for cardiac disease There are however a number of situations in which diagnostic error may arise (page 115) Asthma especially when continuous may at times lead the clinician wrongly to diagnose a heart disease that does not exist Again the asthma may so dominate the picture that an associated cardiac lesion is overlooked In yet other patients the asthma is so overshadowed by the heart trouble as to be overlooked

## ILLUSTRATIVE CASE

Here is a case in which heart disease was wrongly suspected in a patient with severe asthma

**Case 96** Mrs C F a white woman 52 years old had had asthma since the age of 11 During the last two years the asthma had been practically continuous The least exertion caused distressing increase of dyspnea Because of nasal obstruction due to polyp she was brought to the office of a rhinologist The rhinologist was so impressed by her

breathlessness on exertion and her marked cyanosis that he promptly sent her to a cardiologist The cardiologist on the other hand finding no evidence of heart trouble either clinically or by electrocardiogram sent her to me for study of her asthma The asthma was greatly relieved by treatment according to allergic principles so that she proved a good subject for nasal surgery and eventually was restored to her usual health The cyanosis which had so strongly suggested heart disease to the rhinologist cleared up when she stopped taking a proprietary asthma medicine containing acetanilid

Severe asthma may for a time mask the development of cardiac disease This is more likely to occur in the elderly and in those with fairly continuous rather than paroxysmal asthma *In part, at least, this is a result of* the masking of physical signs in the heart by the overexpanded and noisy lungs The chance for diagnostic error will be lessened if the physician makes it customary to examine the heart at a time when epinephrine has minimized the asthma but when the pressor effects of the drug are wearing off

Asthma is not always a clearly defined condition with obvious symptoms and findings In its milder forms the patient experiences nothing beyond a tendency to bouts of coughing and a slight feeling of tightness in the chest Such symptoms may last only a few minutes after being provoked by exertion or hearty laughter Or they may be more prolonged and are then considered as colds, to which the patient casually refers as his 'cigarette cough or his 'bronchial trouble Physical examination would disclose a few wheezy rales at the height of symptoms but would be negative in the intervals Neither the patient nor his physician thinks of the condition as a true allergic asthma Yet such it is and at any time it may assume major proportions and serious significance especially when heart disease enters the picture Its recognition then becomes a matter of vital importance

## ILLUSTRATIVE CASES

Examples of this are furnished in the following abstracts of cases reported by me elsewhere [184]

**Case 97** C S a man aged 53 was admitted to the University Hospital because of dyspnea and edema of the feet and legs Dyspnea had begun two years before and gradually increased until he had an attack of bronchopneumonia 14 months before admission Following this the breathlessness became much worse at first on exertion then without effort especially toward nightfall Increasing palpitation and peripheral edema caused him to consult a physician who diagnosed heart trouble and gave him digitalis There was no personal or family history of asthma or any other allergic condition For 16 years he had worked in a very dusty occupation; during the last three *years he had been required to wear a mask*

PHYSICAL EXAMINATION showed obvious dyspnea cyanosis edema advanced emphysema a greatly enlarged heart with feeble sounds and a rapid rate a swollen liver and many musical wheezing rales in both lungs The roentgenogram showed enormous enlargement of the heart and probable pneumoconiosis The electrocardiogram gave evidence of severe myocardial trouble There was no eosinophilia

Discussion A diagnosis of advanced emphysema pneumoconiosis and severe myocardial disease with congestive heart failure seemed to offer an adequate explanation for this symptom picture But the wheezy character of the rales aroused the suspicion of allergy On being tested he was found highly sensitive to feathers Avoidance of feathers was followed by marked improvement for a month Then the signs of heart failure gradually returned and the patient finally died The wheezy rales however, did not recur Had the asthmatic component been recognized much sooner, it might have served to delay the eventual failure of the heart

Case 98 W P a man of 51 had complained for two years of cough and hoarseness later of increasing dyspnea worse on exertion and finally of substernal pain Studies established a diagnosis of syphilitic aneurysm of the aorta and a paralysis of the left vocal cord There was no history personal or familial of allergic disease and the blood showed no eosinophilia From time to time however there were wheezy rales in both lungs and it became evident that his aneurysmal symptoms were worse when the wheezy rales were present Skin tests disclosed sensitivity to feathers wool and horse hair Avoidance of these substances resulted not only in disappearance of the rales but also in striking improvement of his aneursymal symptoms and undoubtedly prolonged his life He died nearly three years later when the aneurysm ruptured

Discussion The finding of musical rales in any patient suffering from heart disease should always raise the question of a co-existing asthma True as it is that not all that wheezes is asthma the fact remains that asthma is by far the most common cause of wheezy rales

At times the moist rales of heart failure may mask or completely replace the musical asthmatic rales The failure to obtain positive skin tests although in itself not an uncommon finding in asthmatics of advanced years still further lulls to rest the clinician s suspicion of an asthmatic condition Under these circumstances the therapeutic effect of epinephrine on the patient s breathlessness may be of diagnostic help The following is an example

Case 99 W S a man aged 65 was admitted to the hospital with chief complaints of dyspnea cough and palpitation For 40 years he had had a chronic cough worse in winter At 48 he had his first attacks of nocturnal dyspnea, which then recurred several times a year usually after catching cold More recently the dyspnea had become less paroxysmal but more or less constant and usually related to exertion or to certain cardiac phenomena For 20 years he had had attacks of fluttering of the heart with tachycardia palpitation precordial distress and in the last few months typical angina For several years he had known that he had a high blood pressure There was no family history of allergy

Physical examination showed a drowsy orthopneic patient cyanotic and with Cheyne Stokes breathing The chest was very emphysematous and there were numerous moist rales at both lung bases The heart was definitely enlarged (transverse diameter by orthodiagram was 16 8 cm ) the sounds were feeble the rate rapid and there were many extrasystoles The blood pressure was elevated The liver was felt 8 cm below the ribs in the midclavicular line and was distinctly tender There was no edema The blood urea nitrogen was 4 mg per 100 cc The roentgenogram of the chest showed the enlarged heart and marked passive congestion of the lungs The electrocardiogram gave evidence of severe myocardial disease In view of the old history of asthma skin tests were made but with negative results The whole picture then seemed to be one of

hypertensive cardiovascular disease with rather acute myocardial failure Venesection and rapid digitalization were discussed by the house officers However in view of the old asthmatic history the attending physician suggested the repeated use of small doses of epinephrine (3 minims) as the first therapeutic measure There resulted marked and rapid improvement in all symptoms In five days the signs of cardiac decompensation had nearly subsided the pulse became normal as did the blood urea nitrogen After four weeks he walked out of the hospital

**Cardiac Asthma** At this point I wish to refer briefly to the syndrome cardiac asthma discussed more fully elsewhere (page 301) It is applied to dyspnea that is purely of cardiac origin is attended by rather sudden pulmonary congestion and edema and so has a distinctly paroxysmal manner of occurrence This condition when produced in the manner described is in no way related to allergic asthma In fact the use of the word asthma in this instance is unfortunate because it leads to unnecessary confusion in the minds of students It must be remembered however that the word asthma in Greek has simply the significance of breathlessness *and is therefore practically synonymous with dyspnea* Today asthma is restricted to a type of dyspnea due to the bronchospasm and mucosal edema of an allergic reaction

**Paroxysmal pulmonary edema** (moist not wheezing rales) may result in occasional instances when an asthmatic with severe cardiac disease is exposed to the things to which he is sensitive Vaughn[370] has directly observed two such cases the excitants being inhaled orris root in one and ingested egg in the other Swineford[371] even suggests that a majority of cardiacs who develop cardiac asthma are allergic In my patient W S cited in case 99, the findings were consistent with a diagnosis of cardiac asthma yet the relief obtained through epinephrine strongly suggests the allergic nature of the attack

It would therefore be wise in every case of cardiac asthma to think routinely of the possibility of an allergic factor in its production

## Principles of Diagnosis

The diagnosis of asthma in cardiac patients differs in no wise from that in other individuals The prime requisite however is an alertness on the part of the physician attending cardiac patients as to the possibility of asthma Especially is such alertness called for when the cardiac phenomena completely dominate the clinical picture as they so frequently do It must always be remembered that probably one in every 75 individuals has or has had asthma and that one in every seven is allergic

A detailed discussion of the diagnosis of asthma is out of place in this text It will be well however to outline the principles involved

**Evidence of Allergy** The possibility that a patient is allergic may promptly be suggested by the fact that he has presented at some time in his life a number of symptoms that may easily be recognized as allergic He may have had frankly paroxysmal dyspnea in attacks that occurred whenever he was exposed to certain things and that were relieved by

epinephrine or ephedrine Other such obviously allergic conditions include hay fever perennial allergic rhinitis (paroxysmal excessive sneezing is as a rule allergic) urticaria eczema food or drug idiosyncrasy commonly also migraine A family history of these conditions further suggests the possibility that the patient himself may have inherited the allergic characteristics

The important thing from the standpoint of the history is that questioning along allergic lines must invariably be a part of the routine of all history taking

Whenever the dyspnea tends to come in paroxysms in a cardiac patient there is an increased possibility that an allergic factor may be involved This is even more true when the paroxysms occur independently of exertion or when they tend to recur at certain times and places

The finding of wheezing rales in the lungs should always raise the possibility of an allergic cause in their production This possibility becomes a decided probability if epinephrine promptly clears up such rales

Having decided on the basis of the foregoing criteria that the patient probably has asthma as well as cardiac disease one has made only the first step in arriving at a complete allergic diagnosis To arrive at such a complete diagnosis requires

(1) **A searching history** that includes all details of his contacts with substances to which he might be sensitive

(2) **A physical examination** which must always include an examination of the upper respiratory tract by a rhinologist using the nasopharyngoscope and transillumination of the sinuses In this way anatomic defects such as a marked deflection of the nasal septum with firm septoturbinal contacts or secondary pathologic changes such as sinus infection and mucous polyps will be found In selected cases subject of course to the limitations imposed by the cardiac disease bronchoscopy is indicated to discover bronchiectasis or bronchostenosis

(3) **Laboratory studies** including roentgenograms usually of the sinuses often also of the chest and in some instances of the bronchial tree after lipiodol instillation

(4) **Complete skin tests** by some one who knows what to test for and how to interpret the results

(5) **Treatment itself is diagnostically important** for it determines not only the significance of the results of the skin tests but may serve to discover causes which the tests failed to find

(6) **Subsequent Studies** Such a complete diagnostic study is not necessarily the last diagnostic survey The fundamental trouble with the allergic patient is not that he has asthma or that he is sensitive to horse hair but that he has inherited the ability to become sensitized to things in his environment more easily than do normal persons Therefore his sensitization pattern is not a fixed and static thing but can and does change in the course of the years old sensitivities disappearing and new ones developing This possibility must therefore be considered when the patient suffers a relapse

### Principles of Treatment

Here again there is no fundamental difference in the management of cardiac patients with asthma as compared with asthmatics who have no cardiac disease There are, to be sure occasional instances in which drug therapy of one condition needs to be modified in consideration of the other The chief of these will be mentioned later

I shall confine myself to a brief outline of therapeutic principles For details as to my views on the subject the reader is referred elsewhere[181]

**Allergic Factors** The first axiom in allergy is that avoidance of that to which the patient is sensitive gives by far the best therapeutic result But to be wholly effective such avoidance must be complete When complete avoidance is impossible or highly impractical (e g house dust or pollen) then one should strive to attain a partial avoidance as great as may be The production of symptoms by an allergen in a sensitive patient is a quantitative matter A very little of the allergen may cause no symptoms at all More allergen will provoke mild symptoms and much allergen will cause serious symptoms The more of the allergen which the patient avoids the more likely is he to be helped by the next therapeutic measure to be applied desensitization by injection of extracts of the things that cause his asthma Sensitivity to pollens and to house dust most commonly calls for such injection treatment In addition to these orris root feathers hair and an occasional occupational dust may call for desensitization when unusual circumstances make their complete avoidance by the patient impossible Food sensitivity calls for desensitization as a rule only in case of the foods hardest to avoid egg milk and wheat and then this is attempted by feeding (rather than by injection) of increasing amounts beginning with quantities too small to produce symptoms

***The Treatment of Complications*** This calls for some consideration of the treatment of the cardiac disease From the standpoint of drug therapy attention is called at this time to two things that should be remembered in the case of allergic cardiac patients Allergic patients furnish the bulk of those who have drug idiosyncrasies These include such drugs as quinine, quinidine salicylates iodides barbiturates and opiates When a patient gives a clear-cut history that he is sensitive to a drug it should never be given except under the greatest need and with the greatest precautions lest the result prove dangerous The second point of warning from the angle of cardiac therapy is that opiates and especially opiates together with atropine drugs so useful in cardiac disease must be used with the greatest caution in patients with intense asthma and greatly reduced and very viscid sputum that is in status asthmaticus Their use in status asthmaticus has been the most common cause for death in asthma

Nasal Complications often call for surgery provided the cardiac condition permits There may be need for a submucous resection the drainage of infected sinuses or the removal of nasal polyps Such operations should

be performed under local anesthesia They should not be done during a pollen season lest the patient develop a new pollen sensitivity

THE TREATMENT OF INFECTION in sinuses or bronchial tree requires careful and sustained treatment In addition to surgical measures to insure drainage of sinuses this includes the use of vaccines autogenous or stock Such vaccine therapy must be very cautiously used especially from the standpoint of dosage lest injections be followed by serious reactions in those sensitive to bacteria Initial doses should never exceed two million organisms and may have to be much smaller Injections are best given at intervals of not less than one week Change of climate especially during the winter months is a valuable measure when feasible

**The Treatment of the Asthmatic Dyspnea** The most effective drug in asthma is of course epinephrine It may be given by inhalation of a vaporized 1 100 solution or the subcutaneous injection of 1 1000 solution Here the doses should be small 2 or 3 minims repeated as often as needed rather than larger doses Epinephrine may be suspended in oil (1 500) or dissolved in gelatin that is solid at body temperature but liquid at a slightly higher temperature The absorption of the drug is thereby delayed and its effect greatly prolonged In the presence of cardiac disease however the use of epinephrine has certain obvious limitations even contraindications These include coronary disease and hypertension in which such a violently acting pressor substance should be used with extreme caution or not at all Less effective and also less dangerous are ephedrine neosynephrine and related drugs These drugs while less useful than epinephrine in severe asthma, are often very helpful in preventing attacks when they are routinely administered several times a day Here again smaller doses e g ⅛ grain to ⅜ grain of ephedrine sulphate should be used to avoid unfavorable effects on heart and blood pressure

IODIDES are of great value in cases of chronic and more or less continuous asthma Small doses 2 or 3 grains t i d should be given by mouth and over long periods

ANTIPYRIN AND ACETANILIDE Some asthmatics have found that they get considerable relief through certain proprietary mixtures containing these two drugs Their use in cardiac patients is to be discouraged because of the danger of methemoglobin formation and consequent impairment of respiratory function

NONSPECIFIC PROTEIN SHOCK THERAPY so useful at times in chronic asthma is contraindicated in the presence of cardiovascular disease notably myocardial weakness hypertension and arteriosclerosis

In more severe attacks *aminophyllin* 2 grains by mouth or far better 7½ grains in 2 cc of solution injected intravenously may relieve when epinephrine fails

IN THE MOST SEVERE ATTACKS *status asthmaticus* one is dealing with a major emergency which calls for prompt and decisive action The first indication is immediate hospitalization if at all possible The patient should be in a room alone not in a ward Bedding and all contents of the room

must be in keeping with his known allergic pattern This must be arranged in advance On several occasions I have saved a patient's life by taking out of his oxygen tent the feather pillow that was choking him to death

Oxygen or Oxygen with Helium, is the most effective means of combating the cyanosis

Anesthetics At times surgical anesthesia has proved life saving I prefer to use avertin, 60 to 80 mg per kilo of body weight given in solution by bowel

Venesection in the presence of pulmonary edema is of recognized value One should remember the principle set forth by the old phlebotomists that 10 ounces rapidly withdrawn was more helpful than 20 ounces removed slowly

**Climatic Treatment** There is no climatic treatment of asthma There is only climatic treatment for the individual asthmatic What may be a favorable climate for one may not prove so for another A few guides in selecting a climate may be ventured but without any advance guarantee of efficacy An equable climate without severe storms is preferable for most asthmatics The asthmatic with cardiac disease should never go to an altitude higher than 2000 feet Those with much bronchitis and considerable sputum will be better off in the dry climate of southern Arizona or southern California On the other hand if the patient's sputum is scant and viscid a moist climate and near sea level is better (Georgia Florida Gulf Coast) High humidity and especially fog are badly tolerated by most asthmatics Whenever a climate change is contemplated care must be taken that the patient does not encounter in his new environment the things to which he is sensitive

From what has been said it is clear that the management of a patient with asthma and cardiac disease requires of the physician a degree of skill and judgment not exceeded in the realm of clinical medicine

# 17

# CARDIAC PROBLEMS IN SURGICAL PRACTICE

## THE SURGICAL RISK

We have advanced considerably since the days when auscultation at the last moment in the anesthetizing room was considered sufficient to determine the risk from the cardiac standpoint Today the functional capacity of the circulation is stressed while the murmurs that attend valvular lesions carry far less weight in the final estimate of the patient s ability to stand the added strain of anesthetic and operation There is also a greater realization today that the circulation is not the simple problem in hydraulics it was once believed to be and the heart is not the only motive organ

**The role of the peripheral circulation** in the production of many symptoms in surgical patients that were formerly regarded as cardiac manifestations is now appreciated A better understanding of the signs and symptoms that accompany surgical shock aids in the recognition of this condition and still further reduces the number of heart deaths reported by surgical services

**A detailed study** of every aspect of the cardiac patient is an essential prelude in the assessment of the surgical risk Here again the classification of the American Heart Association (page 59) proves most useful in assembling the essential details for only when the cardiac diagnosis is summarized under etiology anatomy physiology and functional capacity is the way paved for consideration of the problem of the surgical risk I have found the small form shown in Table XI a handy guide in these cases If filled out by the surgeon and internist before the consultation it will sharply outline the situation and save considerable time

Response to Exercise A knowledge of the heart s response to the exercise imposed by daily activities will aid in giving an opinion as to its probable conduct during anesthesia and operation Many times the burden imposed by operation is far less than this accustomed load Consequently if the patient tells us that he has no dyspnea or chest pain on ordinary exertion we can be reasonably sure that the functional capacity of the heart will not be dangerously taxed by the operation The few exceptions to this rule are the usual unpredictable types coronary disease with angina and syphilitic aortitis Sudden death of patients in these groups may occur during surgical procedures just the same as it may occur during the ordinary activities of every day life but fortunately this is a rare event

TABLE XI

*PRE-OPERATIVE CARDIOVASCULAR CONSULTATION SHEET*

*Name* *Age* *Service of*

Occupation
Surgical diagnosis
Operation contemplated
Last medical history (resume)
Family history of cardiac disease

THE CARDIOVASCULAR STATUS

Symptoms

Dyspnea or chest pain (check)— { On level / On grade / On stairs / On hurrying / Against the wind }

Cardiac pain— { Location / Duration / Radiation }

Duration of above symptoms?
Are they stationary or progressive?
Is cardiac failure present? Edema? Its extent

EXAMINATION OF THE CARDIOVASCULAR SYSTEM

General appearance
Blood pressure Systolic Diastolic
Venous pressure
Peripheral vessels (check) Barely palpable Thickened
Tortuous Calcified
Retinal vessels (if examined)
Heart
Size (record position of apex beat if palpable)
Thrill (location and time)
Heart sounds (intensity splitting)
The rhythm
Murmurs (location transmission in erect position and in recumbency)
Response to previous operations
Response to exercise test
Result of electrocardiographic study
Result of chest roentgenogram or fluoroscopy
Orthodiagram

Cardiovascular diagnosis (A) Etiologic
(B) Anatomic
(C) Physiologic
(D) Functional capacity
Therapeutic Class

The grade of risk
Result of operation
Cardiovascular condition on discharge
Cardiovascular prognosis

Patients who have complete heart block should be judged on the basis of the myocardial reserve Usually they cannot carry on ordinary activities of life without discomfort and are poor risks Well compensated rheumatic and hypertensive hearts usually stand anesthesia and operation very well When rales are present in the lung bases or other signs of congestive failure can be demonstrated the patient is a poor risk and should not be operated on until the congestion clears, and then only if the situation

without operation is an immediate threat to life itself An estimation of the grade of cardiac risk based on a study of the patient s functional capacity may be obtained by the application of the data summarized in Table XII

TABLE XII

THE GRADE OF RISK BASED ON A STUDY OF THE FUNCTIONAL CAPACITY

| | | |
|---|---|---|
| Grade I | Class 1 of American Heart Association (New classification) | Good risk Here are included patients in whom ordinary physical activity does not cause undue fatigue palpitation dyspnea or chest pain all cases of well compensated valvular heart disease except syphilitic hypertensive heart disease with no renal involvement |
| Grade II | Classes 2 and 3 of American Heart Ass ciation | Risk fair with careful medical supervision and pre operative treatment Emergency surgery only until risk improved Here are grouped cases of beginning congestive failure and angina The e cases all show undue fatigue palpitation dysp nea or chest pain on *ordinary* physical activity |
| Grade III | Cl ss 4 of American Heart Association | Surgery contraindicated These patients show signs of cardiac insufficiency at rest or signs of heart infection They cannot carry on *any* physi cal activity without discomfort Here are in cluded severe angina patients cases of cardiac decompensation with edema and severe dyspnea and patients with marked reduction of the myo-cardial reserve |

**Type of Surgical Procedure** Finally, an estimation of the surgeon s ability in performing the contemplated operation and the probable duration of the procedure must be considered Certainly the patient who is on the operating table for three hours is not as good a candidate for recovery as the patient who is back in his room in half this time following the same operation provided an equal delicacy of tissue manipulation has been shown

## THE VALUE OF THE ELECTROCARDIOGRAM

The electrocardiogram is rarely the sole basis for estimating the surgical risk except in the presence of unusual arrhythmias or when coronary occlu sion is suspected However the electrocardiogram may be of indirect as sistance in evaluating the cardiac prognosis which will aid in making the decision regarding operation Many operations of convenience like hernior rhaphy and hemorrhoidectomy are not carried out in cases where the electrocardiographic findings point to a very serious lesion that is usually not compatible with more than a year or two of life The electrocardiogram may also ease the surgeon s worries by identifying a number of cardiac arrhythmias as harmless types THE ELECTROCARDIOGRAM IN ITSELF OFFERS NO SHORT CUT TO AN ESTIMATION OF THE SURGICAL RISK It is only a part of the cardiac examination and should be considered with the rest of the clinical and laboratory data in making the evaluation (Table XI)

Occasionally the electrocardiogram may be a great assistance to the sur geon in differentiating coronary occlusion from acute abdominal emergen cies when the pain is referred to the abdomen (page 479)

## Choice of Anesthetic

If care is used in the choice of the anesthetic and the anesthetist no untoward effects on the heart need be feared Although disturbances of cardiac rhythm during induction as well as fall in the blood pressure and cyanosis are often noted we cannot blame the heart for what is often the result of a poorly administered anesthetic If a sudden increase in the pulse rate that attends the onset of a paroxysm of tachycardia occurs during anesthesia, this should not be a cause for alarm if dyspnea and venous stasis are absent Vagus pressure often stops the attack, and it is rarely necessary to resort to emergency measures (page 383)

Electrocardiographic studies made during operation on 109 patients by Kurtz and his coworkers[171] showed marked changes in the rhythm Sinus arrhythmia extrasystoles, downward displacement of the pacemaker were the most common alterations although paroxysmal auricular fibrillation and heart block were recorded in rare instances Chloroform was found to produce the greatest number of irregularities and procaine the least The association of chloroform with instances of ventricular fibrillation has likewise seemed to decrease the frequency of its use in modern surgical practice

Care should be exercised in the use of epinephrine combined with the various preparations used in local anesthesia in patients with coronary disease and angina since instances of coronary occlusion following operation have been traced to this source Epinephrine may also provoke ventricular fibrillation in susceptible cases if not used cautiously

Nitrous oxide oxygen if skillfully given is satisfactory for cardiac patients However if the situation is not in the hands of a well trained anesthestist ether, using the open drop method, is safer

### CARDIAC ARREST DURING ANESTHESIA

The sudden stoppage of a normal heart during the administration of an anesthetic is an emergency that has a happy ending in few instances Considering the advances made in the experimental laboratory and the recent successful defibrillation of the human ventricles by Beck prompt action by previously trained resuscitation squads should bring success in a much higher percentage of cases

**Ventricular fibrillation and cardiac standstill** are the terminal mechanisms that must be combated In 1850 Hoffa and Ludwig first showed that electrical stimulation of the mammalian heart produced ventricular fibrillation and death Provost and Battelli, in 1899 succeeded in applying a countershock directly to the fibrillating heart by placing electrodes on its surface and bringing about complete standstill Hosker Kouwenhoven and Langworthy in 1933 demonstrated that adrenalin and calcium chloride after the countershock and standstill restored the normal beat Wiggers used massage before applying the countershock

and has been successful in re establishing normal rhythm in dogs with fibrillating ventricles

Mautz emphasizes the importance of adequate pulmonary ventilation while attempts are being made to revive the fibrillating ventricles A supply of oxygen can be delivered to the lungs by the use of a face mask or an intratracheal tube Direct massage of the heart moves the oxygen from the lungs to the brain tissues where the lack of oxygen produces irreparable damage in three to five minutes A chest incision with removal of one or two cartilages should be quickly done and the heart grasped in the hand In this manner the heart may be emptied and circulation continued

**The process of defibrillation** should next be attempted Mautz working in Beck s laboratory has demonstrated that procaine hydrochloride is useful in the defibrillation process by reducing the irritability of the heart Two cc of a 5 per cent solution are injected into the right ventricular cavity Massage of the heart forces the drug into the coronary circulation and the cardiac tone is quickly reduced When an electric current of 1 0 to 1 5 amperes is then sent through the heart by placing two electrodes directly on its surface the fibrillation is usually replaced by standstill At this stage 1 cc of a 1 to 1000 solution of epinephrine hydrochloride well diluted and added to a 5 per cent solution of calcium chloride is injected into the right ventricle and massage continued Co-ordinated contractions of the heart are now initiated in many cases although small subsequent doses of epinephrine may be necessary To guard against dilatation the heart should be carefully watched for 20 minutes before the chest is closed A team possessing the knowledge of the essential apparatus and the technic to employ in using the drugs that have been recommended by Beck and his associates in the defibrillation of the human ventricles should be available to every surgical service

**Other Procedures** In the absence of the team and equipment necessary to defibrillate the ventricles either of two procedures may be employed The heart may be massaged through the diaphragm and in this manner a flow of blood to vital cerebral centers maintained or intracardiac injections may be used The combination of these two methods is more apt to be successful but the results will not equal application of the more accurate measures outlined above

Drugs Any of the numerous drugs that have been recommended for cardiac injection may suffice in cases of standstill if they are capable of producing an irritable ectopic focus at the site of injection [168] In the first stage of anoxemia there is a failure of impulse formation at the S-A node The piercing of the heart muscle itself is a stimulation and is followed by a cardiac contraction and the re establishment of normal rhythm In a later stage of anoxemia when the heart muscle is pierced by the needle it sends out a series of stimuli cau ing a paroxysm of tachycardia which is of the ventricular type if the mu cle of the ventricle is pierced or a paroxysm of auricular flutter if an auricular area is injected Hyman[169, 170] points out that the important difference between these mechanisms in the second

stage of anoxemia is that paroxysms of ventricular tachycardia or flutter nearly always end in fibrillation and death, while paroxysms of auricular flutter lend themselves to treatment CONSEQUENTLY, IT IS FAR BETTER TO INJECT THE AURICLES IN AN EMERGENCY The right auricle is preferable and is just as accessible as the ventricular site The right auricle is entered by inserting the needle in either the third or fourth intercostal space just to the right of the sternum

### CAN THE SURGICAL RISK BE IMPROVED?

Co-operation of the surgeon and internist makes possible the improvement in the risk by proper pre-operative treatment in many cases Early congestive failure calls for delay in operation until it is controlled by the usual measures of rest and digitalis Recent studies also show the practical importance of biochemical considerations in improving the surgical risk Hypochloremia hypoproteinemia, as well as vitamin B deficiency (Chapter 21) influence edema in these patients and may increase the hazard of operation regardless of the technical skill of the operator The same rule applies to the delivery of patients in obstetric practice

Pre-operative digitalization is indicated only in the presence of congestive failure or auricular fibrillation Some surgeons still prescribe digitalis routinely before operation in all cardiac cases even though the patient shows no circulatory symptoms in carrying out the ordinary activities of life If this evidence of good circulation is present, how can it be further improved by the use of digitalis? The belief still exists that digitalis is useful in sustaining blood pressure and in increasing myocardial tone ' This it does not do, neither does it prevent hypostatic pneumonia in old people following operation On the other hand there is evidence that digitalis administered routinely before operation in the absence of cardiac failure may contribute to a fatal cardiac accident (page 86)

### POSTOPERATIVE CARDIAC ACCIDENTS

In patients who have cardiac disease of the coronary type with angina the possibility of an accident under the surgeon s care is the same as it is in the medical ward However, if convalescence from operation is complicated by sepsis or pneumonia these factors may precipitate an occlusion When surgery is imperative in the midst of an attack of coronary thrombosis, which is fortunately rare, the mortality rate will be high Sudden death following major surgery in patients who have syphilitic aortitis cannot be prevented

Another cause of death during the postoperative period is congestive failure Embolic and cerebral accidents occur more frequently in these patients with impaired circulation As a general rule all cardiac cases react badly in the presence of postoperative infection or pneumonia Congestive failure can be made an insignificant cause of postoperative deaths only when recognized and promptly treated before operation

## CIRCULATORY PROBLEMS OF SURGICAL IMPORTANCE IN THE DIAGNOSIS OF ABDOMINAL LESIONS

Abdominal symptoms may be produced by almost any of the etiologic types of heart disease previously discussed (Table XIII) The mechanism of the production of the symptoms however is variable For example the failure of the heart as a pump causing congestion of the abdominal organs is usually first reflected in enlargement of the liver Rheumatic heart disease with mitral stenosis is present in over 50 per cent of these cases although hypertensive or arteriosclerotic heart disease may be the cause Cardiac failure may produce the symptoms usually encountered in gastro-intestinal–tract disease—gas anorexia nausea vomiting diarrhea fulness

TABLE XIII

CLASSIFICATION OF CIRCULATORY DISTURBANCES OCCASIONALLY PRODUCING ACUTE ABDOMINAL SYMPTOMS

(1) Cardiac Failure
- (A) Congestive Type
  - Liver Enlargement (right upper quadrant pain)
  - G I Tract Congestion (nausea vomiting gas hemorrhage etc)
- (B) Coronary Type (reflex)
  - Angina (pain referred to upper abdomen)
  - Coronary Occlusion (similar mechanism)

(2) Pericarditis
- (A) Acute Pericarditis (pain at times referred to abdomen)
- (B) Calcific Pericarditis (cardiac compression) Ascites may be an early symptom

(3) Embolism and Thrombosis
- (A) Mitral Stenosis (auricular fibrillation) Emboli from large left auricle to splenic renal superior and inferior mesenteric arteries and to bifurcation of aorta and iliacs
- (B) Subacute Bacterial Endocarditis Infected emboli from left side of the heart Same locations as above

(4) Organic Vascular Changes
- (A) Aortic Aneurysm
  - (a) Symptoms produced by tumor growth
    - Displacement of organs
    - Vertebral erosion
  - (b) Symptoms produced by rupture or dissection
- (B) Arteriosclerosis Spasm (abdominal angina)
  - Hemorrhage (in hypertension)
  - Thrombosis
- (C) Periarteritis nodosa.

and pain in the abdomen and loss of weight Mild yet clinically detectable degrees of jaundice may be added to the symptom of right upper quadrant pain caused by sudden distention of the liver capsule completing the masquerade [314] Ascitic fluid in small amounts may arise further to complicate the picture In some cases if constipation is present with the congestive failure this distention of the colon may reflexly inhibit the flow of bile from the liver as well as cause hypertonicity of the sphincter of Oddi Biliary dyskinesia follows [134]

Compression of the heart in calcific pericarditis by the decrease in dias

tolic filling may produce signs of venous engorgement, and the large liver and ascites may first attract attention to the condition (page 181)

**Embolism** In certain types of heart disease, embolism is a frequent mode of production of confusing abdominal symptoms Again patients with mitral stenosis and enlargement of the left auricle constitute the majority of this group Subacute bacterial endocarditis, with its tendency to involvement of the left side of the heart, is likewise a dangerous threat to the integrity of the arterial circulation below the diaphragm Emboli in vessels supplying the abdominal organs may be responsible for the sudden onset of symptoms simulating a variety of surgical lesions Occlusion of the mesenteric vessels presents a picture often diagnosed intestinal obstruction while a diagnosis of renal calculus may be made when an embolus lodges in the kidney

**Referred pain** from coronary-artery disease with angina or more frequently occlusion may simulate any type of gastro intestinal tract disturbance The abdominal reference of pain in cases of angina and occlusion, and infrequently in cases of acute pericarditis may simulate gall bladder disease ulcer or acute pancreatitis Similarly, reflexes from these organs may at times produce changes in the cardiac rhythm and even in the form of the electrocardiogram Recent experiments upon dogs by Owen[797] and Crittenden and Ivy[79] have served to prove that this mechanism is more than a mere possibility Stimulation of the vagus nerve by disturbances in the gallbladder is no doubt the fundamental cause

**Palpable abdominal masses** caused by aneurysmal dilatations of the abdominal aorta particularly when they occur in women, are puzzling to the surgeon Rupture or dissection of the aneurysm produces an acute picture rarely correctly diagnosed and often leading to an unnecessary celiotomy Smaller hemorrhages although productive of the same degree of confusion may occur in abdominal organs in hypertension Arteriosclerosis of the abdominal vessels may lead to thrombosis and the clinical picture will depend upon the size and location of the vessels involved Reduction of the blood supply in the absence of thrombotic occlusion may give rise to abdominal symptoms that have been grouped under the clinical heading of abdominal angina Lack of proper blood supply (ischemia) when the demand on the gastro intestinal tract is greatest (after meals) produces pain

## ILLUSTRATIVE CASES

### Coronary Heart Disease Complicated by Acute Coronary Occlusion with Abdominal Reference of Pain

**Case 100** Mr J M., a mechanic age 50 was admitted to the College Hospital July 6 1938 with chief complaint of sudden severe epigastric pain coming on while at work He gave a history of two years treatment for gastric ulcer No roentgen ray study however had been made

Physical Examination The patient showed marked pallor and was sweating p o

fusely Pulse 100 temperature 97 F and respiratory rate 30 The heart was not enlarged B P 110/70 There was upper abdominal tenderness but no rigidity

Laboratory Data W B C 12 000 The first electrocardiogram was negative A second electrocardiogram taken a few hours later showed characteristic T wave changes of coronary occlusion

Discussion The previous digestive tract disturbances complained of by this patient were no doubt secondary to the coronary lesion He suffered from a vague type of indigestion for some years and although he was never fully studied to prove the diagnosis of peptic ulcer it was assumed that this lesion was present because of the favorable effect of alkali therapy The history of this form of treatment centered the attention of the receiving ward physician on the gastro-intestinal tract the diagnosis of ruptured peptic ulcer was made and the patient was placed on a surgical service It is a matter of additional interest in this case that the usual leads of the first electrocardiogram were entirely negative and the typical electrocardiographic pattern did not appear until 18 hours after the onset of the attack At the same time a friction rub was heard over the precordium clinching the diagnosis It appears that the dangerous period for these cases in which there is abdominal reference of pain is the silent interval between the onset of the attack and the development of the typical electrocardiographic signs

Coronary Sclerosis Followed by Acute Coronary Occlusion Diagnosed Gallbladder Disease

Case 101 N M a male clerk of 51 when first examined complained of indigestion gas and occasional pain in the upper abdomen Dyspnea and palpitation had been present for years No edema or chest pain The significant findings were obesity slight increase in blood pressure (164/94) occasional premature beats but not much increase in heart size The electrocardiogram (Fig 154 A) showed only a left axis deviation The patient was placed on a dietary regime and told to make arrangements for a gallbladder roentgenologic study This he failed to do and when next seen 15 months later he showed no improvement The indigestion was worse the dyspnea was increasing and he stated that a week before the second examination he had experienced a very severe attack of indigestion This attack came on at night awakened him from his sleep and required a hypodermic injection of morphine for relief Another electrocardiogram (Fig 154 B) showed the presence of a recent coronary occlusion of the posterior type

Discussion Many times in patients of this age and build gallbladder disease and coronary disease coexist This association has led to a great deal of discussion and much speculation in the literature The exact relationship between a diseased gallbladder and the heart remains a complex subject although electrocardiographic evidence of improvement has been observed to follow cholecystectomy as will be shown presently Many investigators have also demonstrated the existence of important reflex pathways between the gallbladder and the heart Even effects upon the cardiac rate and rhythm have been shown to occur at the time of operation It has been my impression in a number of cases where striking postoperative improvement in the pain has been observed that the initial opinion as to the degree

of coronary involvement was incorrect In other words, most of the symptoms were produced by disease in a high lying gallbladder

If this is true our chief concern therefore lies in the correct identification of the major lesion The pain of acute coronary occlusion is often confused with the pain produced by gallstones and a celiotomy performed [10, 11] Pain, vomiting, fever leukocytosis are commonly met with in both conditions However, if the past history is carefully reviewed the patient with gallbladder disease will usually show a history of indigestion, while the

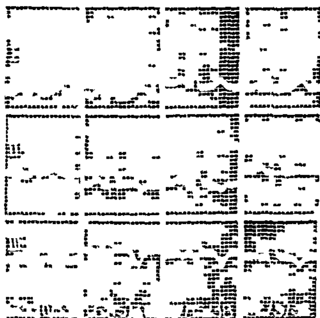


Fig 154 The electrocardiogram 3/20/37 shows left axis deviation 6/15/38 shows deep Q 3 and domed RS-T Intervals in leads and 3 (posterior coronary occlusion) The subsequent studies show a return of tracing toward normal Q 2 and Q 3 persist

patient with coronary occlusion may give a history of mild attacks of angina on effort A complete cardiac study, using the form suggested (see Table XI) will seldom fail to throw light on the correct diagnosis The degree of shock usually observed in coronary occlusion is not present in gallbladder disease nor is the sharp drop in the blood pressure so constant in gallbladder colic as it is in coronary occlusion The appearance of a friction rub over the precordium clinches the diagnosis in favor of anterior occlusion while the appearance of jaundice swings the balance toward gallbladder disease

Cholelithiasis may cause certain changes in the rhythm of the heart reflexly through the autonomic nervous system Inhibition of the heart can also be caused by stimulation of the filaments of the vagus arising from the wall of the gallbladder Heart block relieved by atropine has been reported

to result from gallbladder stimulation The jaundice produced in some patients by gallbladder disease may affect the cardiac mechanism in some instances

BILIARY TRACT DISEASE AND CORONARY DISEASE—MARKED IMPROVEMENT IN CARDIAC STATUS FOLLOWING CHOLECYSTECTOMY (DR I S RAVDIN)

**Case 102** * H B male age 45 when first examined on 4/1/35 gave a history of several attacks of typical biliary colic over a period of 18 months For approximately three years before admission there was in addition a history of dyspnea and a sense of substernal oppression following moderate exertion A roentgen study revealed the presence of gall stones and the electrocardiogram showed a flat T wave in lead 1 (Fig 155 A) A cholecystectomy was performed on 6/15/35 Convalescence was smooth and uneventful Eight months later the patient reported that he was in an excellent state of health Both cardiac and biliary tract symptoms had entirely disappeared This improvement was reflected in the electrocardiogram taken at this time which showed an upright T wave in lead 1 (Fig 155 B)

**Case 103** Mrs B S an American housewife of 56 was well until nine months before admission At this time she had her first attack of epigastric and substernal pain A diagnosis of calculous cholecystitis was made and during the next six months she had a good deal of distention flatulence and heartburn At the end of this period there occurred another severe attack of epigastric pain again followed by several months of marked indigestion The patient lost 20 pounds in weight and could only be kept comfortable on a liquid diet Cholecystogram revealed abnormal function with multiple stones in the gallbladder An electrocardiogram (Fig 156 A) made on 3/1/36 showed slurring of the QRS complex and inversion of the T waves in leads 2 and 3 which was interpreted as evidence of myocardial damage Cholecystectomy was performed the next day Convalescence was entirely uneventful On 5 1 36 a follow up examination revealed that the patient was in excellent condition with no recurrence of any of the pre-operative symptoms An electrocardiogram showed an essentially normal picture (Fig 156 B)

*Discussion* In 1908 Babcock called attention to the frequency of co-existing cardiac disease and biliary tract disease and three years later this association was further elaborated by Riesman It was the opinion of Babcock and Riesman that the cardiac disease was due to myocardial changes brought about by primary infection in the gallbladder wall In 1931 Schwartz and Hermann called attention to the fact that obesity was frequently associated with biliary tract disease and that the cardiac abnormalities might be due simply to the myocardial changes that accompany this condition More recently it has been suggested that certain of the disturbances in cardiac rhythm in patients with gall stone disease may be purely reflex in character from this focus

The frequency with which improvement in the patients cardiac function has been observed after cholecystectomy for gall stone disease the disappearance of various types of arrhythmias the improvement in the associated anginal syndrome and the return to normal of the electrocardiogram after competent biliary tract surgery has convinced many clinicians that

* Cases 102 and 103 presented and discussed by Dr I S Ravdin Professor of Research Surgery University of Pennsylvania

gall stone disease at least adds an additional load to an already handicapped heart

Fitz Hugh and Wolferth[10] several years ago called attention to the fact that patients with gall stone disease who exhibited cardiac symptoms,




Fig 155 Fig 156

Fig 155 The electrocardiogram before and after cholecystectomy Note increase in amplitude of T and return to normal of the T waves in leads 4 and 5 (Old direct leads)

Fig 156 The electrocardiogram before and after cholecystectomy A change is seen in T and T of the indirect lead

often of the anginal type were greatly benefited following the removal of gall stones from the gallbladder or common duct The patients they reported were found to have abnormal electrocardiographic tracings chiefly

flat or inverted T waves in the first two leads Not only were the patients relieved of their biliary tract symptoms but these observers found that the electrocardiographic changes were reversible within a short period after the biliary tract operation These studies point to a toxic effect of the diseased gallbladder on the myocardium

It should also be remembered that gall stone disease may coexist with coronary disease in patients who have had one or more acute occlusions In a group that now numbers 68 patients who were found following complete studies to have evidences of moderate or severe myocardial disease we have been impressed with the improvement in the cardiac status following the eradication of gall stone disease It may be that the chronic gastric distention and interference with gastro-intestinal motility which so many of the biliary tract patients show plays a part in accentuating the pre-existing cardiac abnormality It has been our experience that patients with gall stone disease who also have heart disease need not be denied operation In the group of 68 patients referred to above where operations were performed for simple gall stone disease or for a stone in the common duct or both there have been but three deaths

## ILLUSTRATIVE CASES

### Abdominal Aortic Aneurysm of Arteriosclerotic Origin Simulating Acute Surgical Abdomen at Time of Dissection Prior to Final Rupture

**Case 104** F F male age 68 had been healthy except for occasional attacks of indigestion until the sudden onset of a tearing pain in the upper abdomen with radiation to the right lumbar region It was accompanied by sweating pallor and vomiting and when the patient attempted to go to the bathroom the slight exertion caused him to fall to the floor in collapse There was involuntary emptying of the bladder and bowel When first seen he was pulseless with rapid shallow respirations The picture was one of impending dissolution The abdomen showed boardlike rigidity and the temperature by rectum was 95 F In 20 minutes the patient regained consciousness and the pulse became perceptible at the wrist A diagnosis of perforated peptic ulcer was made and operation advised Further observations however changed this diagnosis when the boardlike rigidity of the abdomen disappeared A mass thought to be an aneurysmal sac was palpated On large doses of morphine and shock treatment there was rapid improvement in blood pressure color and pulse volume for 16 hours At the end of this time there was a recurrence of severe abdominal pain again accompanied by signs and symptoms of profound shock Boardlike abdominal rigidity did not reappear and the aneurysmal sac was distinctly felt It was more tender and larger in size and there was a bulging in the right flank The patient showed increasing pallor and died in coma two hours later

Autopsy showed no peptic ulcer but advanced atherosclerosis of the aorta an abdominal aortic aneurysm with rupture The entire right side of the abdomen from the spinal column to the lateral wall and from the liver to the pelvis was filled with massive retroperitoneal clot that pushed the posterior peritoneum so far forward that it was nearly in contact with that of the abdominal wall The hemorrhage had pushed into and split the mesentery of the cecum and ascending colon The mesentery of the small bowel was not affected The kidney ureter adrenal gland and other retroperitoneal structures floated in the enormous clot

Retroperitoneal Space and Structures The aortic wall was thin and inelastic and the intima was pitted and cracked with atheromatous ulcers Just distal to th origin of the superior mesenteric artery, extending to and involving the bifurcation was a large fusiform dilatation which projected forward and to the left into th abdomen After removal this measured 14 × 8 × 6 cm The root of the mesentery lay across its anterior surface When opened the forward bulging portion was found to be filled with layers of dense yellow fibrin The wall was continuous with that of the aorta overlaid and reinforced by peritoneum and its connective tissue to which it was closely adherent The lumen of the vessel which went through the mass against the posterior wall was lined by a smooth red layer of fresh thrombus In the central portion of this thrombus was a small fissure which overlaid a short (1 cm) irregular rupture in the posterior wall of the aorta

**Discussion** Abdominal aortic aneurysm is a rare yet important consideration in the differential diagnosis of the acute surgical abdomen *Symptoms arising from its rupture or dissection often confuse the surgeon* in the diagnosis of abdominal emergencies puzzle the urologist when small hemorrhages invade the tissues about the kidney or press on the ureter and frequently tax the diagnostic acumen of both internist and neurologist in interpreting pain referred to various sections of the body

It is surprising how large these aneurysms may become and how great a displacement of the abdominal organs they may cause and still elude clinical detection if the sac points posteriorly and does not erode the vertebrae Thompson reported an abdominal aneurysm in a laborer age 39 which contained six and one half quarts of fluid blood and clots at autopsy The aneurysm had pushed both kidneys so far forward that they were diagnosed as metastatic masses on palpation This patient had not consulted a physician until the last few weeks of life Many cases reported in the literature were not seen until they had become moribund following perforation or dissection When subjective symptoms from these cases are tabulated, the most frequently recorded is pain It may be of any variety from a vague type of abdominal discomfort occurring at times in patients before rupture to the typical agonizing terminal variety attending the tearing of the aortic wall The type of pain experienced by the patient in these vascular accidents is outstanding Extremely large doses of morphine seem ineffective in such calamities and this alone should suggest an abdominal vascular complication The ensuing symptoms of profound shock add further evidence Many times in the cases reported in the literature preliminary smaller ruptures may precede the final event The intermittent hemorrhages confuse the picture, and often unnecessary surgical exploration is undertaken The distribution and character of the pain at the time of rupture depend on the location of the aneurysm and *the point of rupture Extravasations into the retroperitoneal* space are frequent If either kidney or the ureter is involved renal colic is simulated and the pain may radiate down the inner aspect of the thigh to the testicle The high site of the rupture as in this case often leads to the diagnosis of perforated peptic ulcer Vomiting and diarrhea are frequently present and serve further to complicate the picture

Figure 157 compiled from cases reported in the literature shows the variety of symptoms that may result from rupture pressure, or dissec

tion when various structures of the body are involved (1) retroperitoneal rupture with perinephric collection simulating abscess (2) pressure on ureter with picture of uremia (3) rupture into the gastro-intestinal tract (duodenum)—pressure on duodenum gives symptoms of pyloric obstructure, (4) rupture into the peritoneal cavity (5) rupture simulating psoas abscess (6) dissection with pressure on iliac arteries followed by gangrene (7) rupture through the diaphragm into the pleural cavity with symptoms of thoracic disease (8) spinal erosion with pain

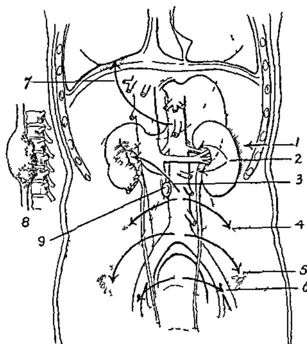



FIG 157 Diagram illustrating organs involved and pathways of dissection in reported cases of ruptured abdominal aortic aneurysm (From New Intern Clin 1 173 1939)

in the back and legs and (9) rupture into the inferior vena cava (arteriovenous aneurysm) Consequently abdominal aneurysms may produce melena hemoptysis or hematemesis Portal splenic- or mesenteric vein thrombosis may occur and give the first clue to the presence of an aneurysm

The clinical diagnosis of abdominal aortic aneurysm rests upon the demonstration of a pulsating expansile tumor mass This sign was present at the time of the second examination of Case 104 Inspection then showed a very slight anterior bulge of the abdominal wall but no pulsations could be seen At times a thrill may be palpable over the suspected mass Palpation carefully carried out usually clinches the diagnosis The tumor mass when grasped shows expansile pulsations as well as upward thrust

and it will seldom be found to move with respirations If the aneurysm is high up under the diaphragm or if it points posteriorly, palpation of the sac may be difficult or impossible Often, on auscultation, a systolic murmur is heard over the sac In some instances, the patient presents himself with the chief complaint of pulsating abdominal mass (described by one patient as an "extra heart") The pulsating aneurysmal sac must be differentiated from the throbbing abdominal aorta and from tumor masses overlying and transmitting pulsations of the aorta In patients where the thickness of the abdominal fat is not too great and the musculature not too rigid differentiation of an aortic aneurysm from a visceral tumor may readily be made if the patient assumes the knee-chest position when the tumor will fall away from the aorta and no longer transmit a pulsation to the examining hand

It is well to remember before making the diagnosis of abdominal aortic aneurysm that a marked pulsation of the aorta is met in cases of extreme anemia in patients with aortic insufficiency in hyperthyroidism and in many underweight neurotic individuals In these cases it may be possible to grasp the vessel in the hand in which event the diagnosis of aneurysm is often made More detailed examination however will always show that only an up and down throbbing is present and no lateral expansile pulsation If the aneurysm is completely filled with clotted blood it may closely simulate a tumor mass and in these cases roentgenologic examination is invaluable Many times roentgenograms will reveal a pressure erosion in the vertebral column between the eleventh dorsal and third lumbar segments and avoid an unnecessary laminectomy

We have encountered abdominal aneurysms three times proving the diagnosis in each instance in 4 058 patients referred to the Cardiac Clinic of the Woman s College Hospital during the past ten years All were encountered in men past 60 years of age and all were of the arteriosclerotic type

For additional cases illustrating the production of abdominal symptoms by other types of circulatory disease see Cases 22 and 26

## TRAUMA AND THE HEART

The effect of trauma on the cardiac structure and function remains a matter of much uncertainty The testimony usually heard in courts of law reflects a wide range of beliefs among physicians and shows the need of further investigations of these important problems

Penetrating wounds of the chest may involve the heart in which event the mortality rate will be high but not always 100 per cent as is the popular belief Nonpenetrating wounds are quite as capable of causing serious cardiac injury and death may follow a blow that leaves no external mark on the chest as evidence The sudden strain of lifting may at times produce cardiac injury Finally and by no means the least important of all the accident may initiate in a patient of the proper pattern

a train of symptoms of psychoneurotic nature that will center about the cardiac mechanism and greatly complicate the situation

**Importance of Cardiac Records** A complete cardiac study should be made in each case whenever cardiac injury is suspected even though a psychoneurotic factor may be evident from the start These records will at least give the examiner something to work on All the abnormalities in the electrocardiogram and the roentgenogram should be studied and carefully listed Of course the question always arises in court as to the presence before the accident of the changes described It is quite possible for heart disease to be present in some patients who may have had no symptoms related to the circulatory apparatus and no antecedent history of disease likely to produce cardiac damage While the increasing efficiency of the medical supervision of all industrial workers particularly those engaged in the dangerous occupations many times affords the opportunity for this comparison yet in the great majority of instances when the question arises as to the origin of some defect of structure or function previous studies are not available Physicians in private practice usually keep poor records and this occasionally deprives a patient who has been in an accident of the opportunity of receiving a just decision when the claim for damages is based on cardiac trauma It is also possible in cases where the heart has been damaged before the accident that a greater degree of traumatic injury may result Records showing the previous cardiac status give an opportunity for comparison especially in cases where an electrocardiogram and orthodiagram have been made before the accident and an excellent chance for evaluation of post traumatic symptoms and signs

When we consider the difficulties that surround the study of many other organs of the body we must confess that cardiac examination is easy The heart can be viewed by means of the fluoroscope against the clear pulmonary background and its mechanisms can be studied accurately by the electrocardiograph Consequently if we always consider the possibility of cardiac lesions following trauma of any type and carefully record all departures from normal the nature and extent of these lesions in time will be much better understood

**Relation to Pre Existing Disease** Trauma may accentuate any type of pre existing cardiac disease For example slight degrees of trauma may be sufficient in cases of coronary arteriosclerosis complicated by occlusion and infarction to cause rupture of the heart It is entirely possible for trauma to be a factor in precipitating attacks of congestive failure in a patient with a delicately balanced circulation Anginal seizures may be brought on in one already subject to them by the nervous upset that accompanies an accident and this attack may be the one that results fatally Among workmen who hold dangerous jobs the sudden onset of angina paroxysmal disorders of rhythm or attacks of cardiac syncope may cause fatal accidents There is much disagreement concerning the likelihood of trauma predisposing to an attack of acute

rheumatic fever or to a blood stream invasion by an organism like the *Streptococcus viridans* with the production of subacute bacterial endocarditis However, we cannot deny the fact that, in a patient who has subacute bacterial endocarditis, even moderate trauma may cause the rupture of a previously damaged heart valve

### PENETRATING WOUNDS

The most common form of cardiac trauma is that produced by knives bullets or fragments from fractured ribs or sternum These cases are surgical if they survive long enough to be brought to the hospital While many penetrating wounds are immediately fatal a small percentage of cases may be saved by prompt recognition and suture Since no time can be lost when the emergency arises every surgical service should have established rules for diagnosis and treatment of these injuries Elkin[91] states that approximately 2 per cent of the penetrating wounds of the chest involve the heart If all cases were considered the figure would no doubt be higher, since this statement is based on cases that survived long enough to reach the hospital In Elkin s series of 22 cases wounds of the heart were produced either with a knife (15 cases) or ice pick (seven cases) Bullet and gunshot wounds are rarely met in hospital practice since death from hemorrhage usually takes place before emergency measures can be applied

#### SYMPTOMS

The patient who has just received a stab wound of the heart usually is unconscious when first seen In some instances delirium may be present The skin is cold the lips show a pallid cyanosis the heart sounds are weak and distant and the pulse is usually absent These symptoms are caused by loss of blood and beginning tamponade of the heart Free bleeding into the pericardial sac follows the wound in the heart wall When a sufficient quantity of blood collects cardiac action is embarrassed diastolic relaxation is incomplete and the venae cavae are unable to empty completely into the right auricle Consequently an increase in the venous pressure takes place which is evident clinically in the distended condition of the veins of the neck and the cyanosis of lips and tongue As the venous pressure increases the arterial pressure drops, and usually blood pressure readings are soon unobtainable If a portable bedside fluoroscope is handy increase in heart size may be seen with an absence of normal pulsations along the cardiac border produced by the accumulation of blood in the pericardial sac If these symptoms of tamponade are demonstrable following a stab wound cardiac suture should be attempted at once Although the patient is unconscious at the beginning of the procedure relief of the tamponade will increase blood pressure decrease venous pressure and re establish cerebral circulation with a quick return of consciousness Consequently, although the patient is comatose at the start an anesthetic should always be used

### PROGNOSIS

The prognosis depends on the speed with which the condition is recognized and operation performed If immediate death from hemorrhage does not occur cardiac tamponade may be quickly fatal while after operation purulent pericarditis and pneumonia often prove serious complications The location of the wound is significant from the standpoint of prognosis In Elkin s series six out of eight patients who had wounds of the right ventricle recovered Left ventricular wounds are more serious only two in this location recovering in the series of 22 cases reported by Elkin Wounds of the pulmonary artery the auricles and intrapericardial part of the aorta have a poorer prognosis because of the technical difficulties involved in successful suture

Rarely some foreign bodies lodge in the heart wall and become encysted others do not remain in one location but migrate until they are free in one of the cardiac chambers in which event embolism may take place The great veins in some reported cases have conveyed foreign bodies to the heart from distant wounds

## Non Penetrating Wounds

Equally serious cardiac injuries can be produced by contusion or compression Beck calls attention to our erroneous conception of the heart as an organ that is well protected by a long thoracic cage whereas in truth it lies against the sternum vulnerable to any sudden blow on the chest and capable of being buttressed against the bodies of the thoracic vertebrae posteriorly

**Penetration of Myocardium** Blows over the precordium may fracture the sternum or ribs and the cavity of the heart may be penetrated by the ends of the fragments A partial penetration of the muscle of the heart may result in healing with subsequent cardiac rupture or the formation of a cardiac aneurysm A cardiac bruise from this type of injury may also heal with the production of subsequent functional disturbances Sudden indirect forces resulting from falls may cause compression of the legs on the abdomen and injure the heart while violent blows on the chest may cause laceration of a cardiac chamber or the aorta and result in sudden death with no external evidence of injury

**In cardiac rupture** the cause of death is neither the injury nor the hemorrhage it usually is cardiac tamponade In a certain number of these cases where the outcome is not immediately fatal careful examination will reveal the tamponade in which event prompt action saves the patient s life RECOGNITION OF THE PRESENCE OF ACUTE TAMPONADE SHOULD NOT BE DIFFICULT IF THE POSSIBILITY OF ITS OCCURRENCE IS ALWAYS KEPT IN MIND WHEN EXAMINING AN ACCIDENT CASE As an emergency measure Beck [4] advises tapping of the pericardial cavity at intervals until operation can be performed This procedure (page 164) serves to confirm the diagnosis and to relieve temporarily the cardiac tamponade

A few months ago I observed one case where the seriousness of the signs of cardiac tamponade were unrecognized following a stab wound of the heart with an ice pick in the fifth interspace about 8 cm from the midsternal line The patient was delirious on admission to the hospital and later pulseless Spontaneous recovery took place without operative interference Such occurrences, however, are rare

SYMPTOMS

**Immediate Onset** Cardiac trauma from non penetrating wounds of the chest may cause symptoms closely resembling those that follow a coronary occlusion If a patient previously in good health receives a blow over the precordium and immediately thereafter develops dyspnea irregularity of the pulse and pain in the chest of the anginal type cardiac trauma should always be considered These symptoms often lead to a diagnosis of cardiac neurosis with which trauma is so often confused If accompanying these symptoms electrocardiographic changes appear that were not observed prior to the accident the presence of a traumatic lesion becomes more than a possibility

*Late Onset In some cases the onset of the symptoms* does not immediately follow the accident instead, the symptoms appear at varying intervals depending on the size location and the progress of the myocardial lesion The latter may result in scar formation but the patient is always liable to develop cardiac aneurysm or cardiac rupture at a later date, particularly if rest is not enforced Contusions of the heart which are productive of large areas of myocardial injury, therefore may in some instances behave quite like cardiac infarcts

**Functional Disturbances** Cardiac trauma may be followed by disturbances of a functional nature including arrhythmias angina and congestive failure

CONGESTIVE FAILURE Either right or left ventricular failure may appear on effort during the post traumatic period, particularly in the presence of an already damaged heart The onset may follow trauma immediately or it may be delayed for some time if the lesion produced in the cardiac structure is of the type that slowly reduces myocardial reserve for example rupture of a valve or prolonged paroxysms of abnormal rhythms accompanied by high ventricular rates Beck's experiments point to the fact that severe contusion of a perfectly healthy heart may at times lead to acute dilatation and decompensation

ANGINA While trauma directly applied to the coronary tree may occasionally provoke symptoms of angina in a normal person the likelihood is even greater if coronary arteriosclerosis is present The nervous shock that results directly from the accident may reflexly cause coronary spasm and in a susceptible person the anginal seizure may appear If chest pain is complained of immediately after trauma and is followed by the sudden death of the patient the effect of the accident on the integrity of the coronary circulation may be strongly suspected Characteristic alterations

in the T waves of the electrocardiogram appearing after the accident lends support to the diagnosis

ARRHYTHMIAS

The appearance of arrhythmias following trauma many times focuses attention on the heart Premature beats or extrasystoles may be noticed for

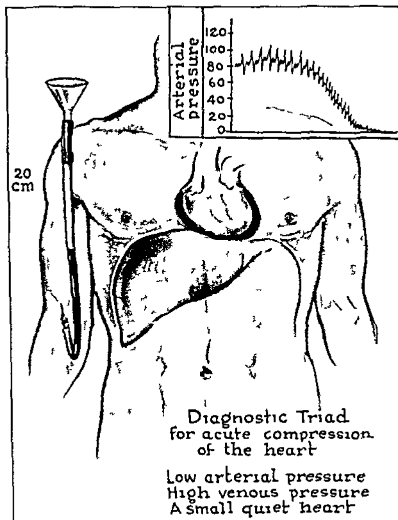



FIG 158 Acute compression of the heart Redrawn from Beck *

the first time after an accident and the more attention is directed toward them the more important they seem to the patient In many instances

* Reprinted by the courtesy of the editor of the American Heart Journal

cardia may be the direct result of myocardial injury and should be promptly controlled because of the tendency of this arrhythmia to terminate in ventricular fibrillation and death

Cardiac injury may bring on an attack of auricular flutter or fibrillation in either normal or diseased hearts If the heart is healthy and not extensively involved in the trauma the abnormal rhythm is usually easily controlled However if the heart is damaged and the arrhythmia is continuous with a high ventricular rate congestive failure may be precipitated

Heart Block Injury to the heart muscle that is followed by hemorrhage in the region of the conduction system may cause varying degrees of heart block Similar lesions have been reported in experimental animals and some case reports in literature point to this occurrence in man To establish this happening beyond a doubt it is necessary to have in evidence a normal electrocardiogram taken before the accident and an electrocardiogram showing the appearance of heart block directly following the trauma

## ILLUSTRATIVE CASE

### Stab Wound of the Right Ventricle—Acute Cardiac Tamponade—Recovery Following Suture

**Case 105** A E an American school boy of 14 was brought to the receiving ward of Memorial Hospital on December 8 1938 by police ambulance approximately one half hour following a stab wound in the left chest with a pocket knife

Physical Examination The patient was unconscious on arrival and showed a pale cyanosis The jugular veins were distended The pulse was imperceptible at the wrist and the respirations were rapid and shallow The heart sounds were faint the rhythm regular and the cardiac rate was 70 The blood pressure could not be obtained by ordinary clinical methods There was a stab wound one half inch long in the fifth intercostal space immediately to the left of the sternum Active bleeding had ceased The liver was not palpable The extremities were cold and pale

Diagnosis Acute cardiac compression (Fig 158)

Indication Immediate operation

Operation (Dr Bruce Fleming) As anesthesia was begun incision was made parallel to the ribs and the wound of entrance completely excised down to the pleura The incision was enlarged and four inches of ribs above and below the incision were removed The pericardial sac was greatly distended contained a puncture wound and was completely filled with a firm blood clot The thoracic cavity contained blood and clots The pericardium was incised through the wound and clots removed Traction sutures of silk were placed in the myocardium, one near the apex centrally and one cephalad to the wound in the heart while bleeding from the latter was controlled by the finger of the assistant The estimated size of the myocardial puncture was three eighths of an inch Two through and through chromic gut sutures were placed in the myocardium completely closing the wound Blood was removed from the thorax and pericardium and strained into citrate solution and returned to the patient intravenously The control sutures were then removed and the pericardium sutured The thoracic wall was closed without drainage Dressings were applied

Course Following operation the patient was placed in an oxygen tent The pulse became palpable as soon as the pericardial sac was opened and the acute cardiac compression relieved At this time the first blood pressure reading obtained was 98/56

A roentgen ray examination mad on the first postoperative day (Fig 159 B) showed a uniform density over th left hemithorax more marked at the base which obscured the lung d tail The heart and mediastinum were d splaced to the right Conclu on Pleural effusion with card ac displacement

An examination made on the fifteenth postoperative day showed a decrease in the effusion The pleural was th ckened and the heart wa still d splaced to the right

A roentgen ray exam nation two months later showed that the left lung had completely re-expanded with absorption of the fluid at the left bas The h art and m diast num occupied normal posit ons

The blood count immediately following operation was hemoglobin 50 per cent R B C 900 000 W B C 14 000 P 8 L 18 Following s veral tran fus ons it was raised to hemoglobin 8 per cent R B C 4 460 000

Electrocardiograms were taken at frequent intervals postoperatively Th changes that took place with healing are shown in Fig 159 C

The patient mad a good recov ry and was discharg d from th hospital s ven w ks after the ope ation

# 18

# CARDIAC EMERGENCIES

While heart disease in most instances gives ample warning of its presence often assuming the form of a chronic illness, situations may arise that demand quick decision and prompt treatment Although these have been discussed fully under their appropriate headings elsewhere in the text, for convenience and quick reference I have attempted to group here the cardiac emergencies commonly encountered with some of the present day views regarding their diagnosis and treatment

Cardiac emergencies are common in surgical as well as in medical practice Many times treatment must be begun before a complete physical examination is made Likewise in some instances the past history is unknown or difficult to obtain in detail Since the leading symptoms must be relieved in some measure before the etiologic possibilities are reviewed it seems appropriate to begin a discussion of emergency treatment with a review of the symptoms of cardiovascular origin that are usually responsible for these calls These are chest pain, dyspnea syncope and palpitation

## CHEST PAIN

Chest pain in cardiac patients requiring emergency treatment may be caused by acute coronary occlusion angina pectoris, pulmonary embolism acute pericarditis, or dissecting aneurysm Angina pectoris and coronary occlusion the complications of arteriosclerotic heart disease are the most common causes The significant features in their differentiation that may prove useful in emergencies are summarized in Table XIV

**Coronary occlusion** is the most frequent cardiac emergency associated with prolonged chest pain and the increasing familiarity of the lay man with the symptoms of this condition usually bring minor episodes promptly under the supervision of the physician The pain of occlusion calls for immediate administration of morphine in sufficient doses to quiet the patient It is best to give an initial dose of 15 mg (¼ grain) and if necessary, repeat the dose in 15 to 20 minutes Quick relief of pain is a major factor in turning the balance in favor of recovery Do not give digitalis unless congestive failure is precipitated If the patient is at home he should be made comfortable in the room where he is found until his condition permits his removal If the seizure takes place on the street the patient should be moved to the nearest shelter to await transportation to the hospital Oxygen therapy if available is an advantage particularly in the presence of cyanosis Injection of concentrated glucose (50 Gm in

TABLE XIV

DIFFERENTIAL DIAGNOSIS IN CHEST PAIN

| | ACUTE CORONARY OCCLUSION | ANGINA PECTORIS |
|---|---|---|
| Appearance of patient | Restless ashen color dyspnea sweating Shock may be present Congestive failure may develop | Patient quiet and immobile Good color No dyspnea No sweating |
| Pulse | Rapid and weak Paroxysmal ventricular tachycardia present occasionally | Normal |
| Blood Pressure | Usually falls to low level Pul us alternans may be observed (page 407) | Normal or elevated |
| Temperature | Subnormal when first seen | Normal |
| Heart Examination | Heart sounds weak and often rapid Gallop rhythm is not uncommon Friction may be *audible if the area of infarction is on the* anterior surface | May be normal |
| Duration of pain | Hours | Few minutes |
| Onset | At any time Common during sleep | Following exertion excitement or overeating |
| Effect of nitrites | Pain not relieved This drug may be harmful | Quick relief usual |

100 cc ) into the arm vein may give quick relief to a failing myocardium Coronary occlusion rarely occurs without pain When it does, other symptoms of collapse of the circulation may appear suddenly especially severe dyspnea (cardiac asthma) The onset of an attack of paroxysmal dyspnea particularly when a previous history of anginal attacks is elicited should always suggest the diagnosis of acute coronary occlusion

**Other Conditions** Herrick[1] has called attention to a number of other conditions that may be associated with chest pain and consequently be confused with acute coronary occlusion He lists under this category effort syndrome cardiac neurosis cardiac arrhythmias pericarditis syphilitic aortitis aortic aneurysm pleurisy pneumonia massive collapse of the lung bronchial carcinoma pulmonary embolism herpes zoster spinal osteo arthritis gall stones peptic ulcer neuralgic or fibrotic causes local to the chest wall hernias through the diaphragm carcinoma of the stomach and tabetic crises

If the chest pain is transient and the patient when first seen by the physician has a good pulse and blood pressure and on auscultation the heart sounds are unchanged angina pectoris rather than occlusion may be suspected A tablet of nitroglycerine 0 6 mg (1/100 grain) under the tongue should bring prompt relief If the pain continues a similar dose may be given in five minutes After emergency relief has been obtained the patient should be advised to have a complete cardiac study made in the near future

**A large embolus** lodging in one of the branches of the pulmonary artery may obstruct the flow of blood from the right side of the heart (acute cor pulmonale) and cause sudden death If the patient is alive when

seen in advanced degree of shock is present The symptoms may then resemble acute coronary occlusion chest pain pallor, thready pulse dyspnea, falling blood pressure and shock The differential diagnosis in some cases may be most difficult if not impossible to make However, the points favoring pulmonary embolism are a recent surgical operation (abdomen or pelvis) fracture, phlebitis, or chronic cardiac disease where an auricular thrombus may have formed An acute cor pulmonale may produce a pulsation in the second or third interspaces just to the left of the sternum occasionally accompanied by a friction rub dilated jugular veins and marked cyanosis Many times these signs are lacking If the patient survives long enough for an electrocardiogram to be made this may help to make the differential diagnosis (see Fig 251) Later cough hemoptysis, and signs of consolidation over the area of the pulmonary infarct may serve to clear the picture

Absolute bed rest morphine oxygen and support of the failing right heart by venesection and if the emergency is extreme intravenous injection of strophanthin comprise measures of value in cases of pulmonary embolism Surgical removal of the embolus is occasionally possible when the accident occurs in the hospital in the presence of a skilled surgical team

**Acute pericarditis** may cause sudden chest pain in younger patients but this is a rare happening The pain usually is caused by the extension of the inflammation to the pleura and diaphragm The age of the patient, and evidences of rheumatic infection serve to differentiate this type of pain from that caused by anoxemia of the heart muscle that occurs in coronary disease

## DYSPNEA

A sudden attack of dyspnea (usually nocturnal) may be the first symptom of heart disease to appear It is the most common cardiac emergency of general practice The patient usually a man is awakened suddenly by a sense of suffocation Dyspnea is present and it quickly increases to orthopnea When the physician arrives he finds the patient's chest full of rales the color ashen and the general appearance one of impending death There may be cough with frothy blood tinged sputum This is the *picture of cardiac asthma or paroxysmal cardiac dyspnea*

**Immediate Treatment** Unless the sudden left ventricular failure is promptly relieved it may terminate in acute edema of the lungs Morphine, 15 mg (¼ grain) given hypodermically and repeated if necessary in 20 minutes is usually most efficient in bringing the attack to an end When pulmonary edema complicates the picture a venesection should be done although venostasis or bloodless venesection may prove helpful The latter procedure consists in applying a tight bandage to the arms and upper thighs close to the trunk to prevent the return of venous blood and in this manner diminish the pulmonary congestion When the attack

subsides the compression bandages are gradually released If the patient is in the hospital when the attack occurs an oxygen tent is useful

When the emergency treatment has been given further observation of the patient who is recovering from a sudden attack of cardiac asthma will usually disclose other evidences of heart disease The victims of these attacks almost always suffer from the effects of a long standing hyper tension and show cardiac hypertrophy chiefly left ventricular In many instances the gallop rhythm of failure may be heard on auscultation in the region of the cardiac apex Pulsus alternans may also appear in these cases If the examination reveals any of these signs a guarded prognosis should be given to the patient s family The duration of life of older patients who have attacks of cardiac asthma is hardly ever over one year from the time of the first attack

**Careful follow up treatment** is recommended in all cases seen in the first attack of cardiac asthma Digitalization should be carried out (page 82) and suitable doses of diuretic drugs particularly the organic mercurial group should be given even in the absence of edema for the effect they often have in preventing the recurrence of the seizures The patient should be told to sleep in a semi reclining position and to avoid slipping down in the bed during the night

**Allergic or Bronchial Asthma** Spells of dyspnea caused by allergic or bronchial asthma in an elderly patient may be confusing at times (page 114) The presence of hypertension and the cardiac findings above described point to a cardiac background particularly if the attacks are of recent origin A history of chronic cough wheezing throughout the day attacks of asthma for many years the presence of emphysema and a recent upper respiratory infection point to bronchial asthma Epinephrine is indicated in the bronchial or allergic type of asthma but is strongly contraindicated in cardiac asthma (Chapter 16)

## SYNCOPE

When the cause of syncope is cardiac the physician obtains his first diagnostic clue from the rate and rhythm of the pulse When no pulse is *felt at the wrist or when it is under 20* beats per minute in an elderly person an Adams Stokes seizure should be suspected Since the auricles continue to beat evidence of their activity should be looked for in the neck veins If regular pulsations can be demonstrated proof of the diagnosis is furnished (page 375) In the presence of an Adams Stokes seizure intracardiac injections of epinephrine should not be used indiscriminately when the exact cardiac mechanism present during the seizure is unknown Where ventricular tachycardia characterizes the attacks the careless use of epinephrine may remove the only chance the patient has of spontaneous recovery (page 403)

**Paroxysmal Tachycardia** The sudden onset of paroxysmal rapid heart action may in some instances be accompanied by a marked diminu

tion in the supply of blood to the brain Syncope follows If an attack of auricular flutter is accompanied by one to one ventricular response the unusually rapid heart rate may be incompatible with circulatory efficiency Paroxysmal tachycardia may likewise produce syncope in elderly patients where advanced sclerosis limits the cerebral blood flow In desperate situations if the patient has not been taking digitalis previously and the paroxysms are accompanied by the sudden onset of congestive failure intravenous use of strophanthin, 0 6 mg (1/100 grain) is justified (page 398)

In paroxysms of tachycardia in young people when no signs of cardiac embarrassment are in evidence less heroic measures suffice (ice water aromatic spirits of ammonia, whiskey taken straight in tablespoonful doses carotid sinus pressure quinidine eye ball pressure, holding the breath bending over with the head between the knees, heat or cold over the precordium) When the patient s condition is good there is no occasion for alarm for the paroxysms of tachycardia are self limiting Recumbency, however should be maintained during the seizure to prevent vertigo or syncope

**Carotid Sinus Syncope** Fainting attacks often accompany hypersensitiveness of the carotid sinus and these may be associated with a slow pulse Recovery is prompt and the diagnosis of the nature of the attack usually offers little difficulty (page 378)

**Emotional Syncope** Certain types of patients are always fainting and sending for the doctor Emotional episodes in the presence of neurocirculatory instability precipitate the attack of syncope A history of previous seizures the good quality of the pulse and the absence of any signs of heart disease on examination suffice to make the diagnosis

**A high vagal tone** associated with sinus arrest may produce syncope (page 379) The treatment is recumbency and atropine

**Aortic Lesions** At times patients with aortic stenosis and aortic regurgitation are subject to spells of syncope Harrison[149] attributes these to an anoxemia that is diffuse involving the left ventricle at the time of increased activity Syncopal attacks occasionally observed in children with patency of the ductus arteriosus may be caused by a similar mechanism since the mechanical effects of this defect are quite like those produced by an aortic regurgitant lesion

**Extracardiac Factors** Syncope is produced many times by factors unrelated to the heart The more common types I shall mention here, since in an emergency a differential diagnosis from heart disease is required Epilepsy can be differentiated from the Adams Stokes seizures on the basis of the tongue biting the character of the convulsive movements and the quality and rate of the pulse during seizures In cerebral accidents the type of breathing and the evidence of paralysis are distinguishing features Sudden hemorrhage may be followed by syncope and this may be accompanied by a rapidly rising pulse and marked pallor

**Thrombi** In mitral stenosis and following a coronary occlusion mural thrombi may form in the heart and these may be swept into the circulation at any time with the sudden appearance of symptoms the nature of which will depend on the distant area affected Vegetations in subacute bacterial endocarditis may likewise become detached with similar sequelae The sudden onset of coma and paralysis should always suggest these complications to the physician who is summoned in the emergency

## PALPITATION

The sudden appearance of palpitation often accompanies one of the abnormal rhythms Initial attacks of paroxysmal tachycardia may cause great alarm on the part of the patient and his family while emergency medical aid is less likely to be sought for the subsequent attacks unless they are unusually severe or prolonged Abnormal rhythms should be differentiated from simple tachycardia The latter is usually present in patients showing other signs that label the episode as purely functional The heart rate while rapid will be noted to decrease gradually Such is not the case in patients suffering from attacks of paroxysmal tachycardia for in these both onset and offset are sudden

**Abnormal rhythms** commonly encountered are auricular fibrillation auricular flutter and paroxysmal auricular or nodal tachycardia Since these mechanisms have already been fully discussed (Chapter 12) only a summary of important data will be included here

Auricular fibrillation when paroxysmal may occasionally be observed in the absence of any other sign of heart disease It frequently accompanies hyperthyroidism If the patient is in good condition and the heart otherwise normal the only therapeutic measures indicated are rest and the administration of a capsule of quinidine sulfate 0 3 Gm (5 grains) If cardiac disease is present and the heart is increased in size particularly if signs of congestive failure are recognized QUINIDINE SHOULD NEVER BE GIVEN If the patient has not previously been receiving digitalis and this fact can be definitely established there is no contraindication to the intravenous administration of strophanthin if the abnormal rhythm is placing a severe strain on the myocardium and early signs of cardiac failure are appearing Enough digitalis should be given subsequently by mouth to maintain the ventricular rate at 70 to 75

A persistently rapid and regular cardiac rate between 130 and 160 beats per minute is more apt to be flutter than tachycardia The breathing the color of the patient and the presence of any signs of cardiac failure should guide the physician in his estimation of the condition of the myocardium and provide a key to the type of emergency treatment to use Here again if evidence is at hand that digitalis has not been previously given full doses may be prescribed to control the ventricular rate The future course of therapy depends on subsequent studies (page 393)

Paroxysmal tachycardia is a common cause of the sudden onset of palpitation in patients who have no other evidence of heart disease The

prognosis in young individuals even in the presence of extremely rapid ventricular rates (160 to 200) is invariably good and death in a paroxysm is practically unknown Normal rhythm may reappear before the physician arrives If so there remain only the effects of the seizure on the nervous system to treat in which event a few doses of phenobarbital suffice If the attack persists the measures previously described may be instituted in order (page 506) A follow up study is needed to determine the underlying cause and to establish, if possible, satisfactory prophylactic treatment (page 382)

## WOUNDS OF THE HEART

Puncture wounds of the heart may be small with the gradual development of a cardiac tamponade by leakage of the blood into the pericardial sac Since many of these cases can be saved by emergency surgical measures (page 494) it is important to act promptly in the presence of the following signs fall in blood pressure rise in venous pressure dyspnea progressing to orthopnea cyanosis tachycardia and decreasing pulse volume They are all produced by a rising intrapericardial pressure compressing the heart and preventing proper diastolic filling

## PERICARDIAL EFFUSION

Occasionally as a pericardial effusion slowly accumulates the symptoms of cardiac tamponade may appear at a much slower rate Nevertheless when the intrapericardial pressure becomes elevated the situation becomes an emergency and prompt treatment may be life saving The technic for aspiration of the pericardial sac is outlined on page 164

## CONGESTIVE HEART FAILURE

In a small number of cases the symptoms of congestive cardiac failure come on suddenly and emergency treatment is needed If digitalis is given under these circumstances to the patient of another physician the amount is gauged by the previous dosage (page 82) If this cannot be determined it is wise to proceed with caution Bed rest and morphine are safer measures to employ Severe dyspnea may be caused by large pleural collections of fluid in which event a thoracentesis may be useful as an emergency measure (page 94)

## CARDIAC RESUSCITATION

Ventricular standstill or ventricular fibrillation are the mechanisms usually responsible for sudden death When either occurs in a badly damaged heart all attempts to restore co-ordinated contraction are futile However as Beck has shown a normal heart that stops suddenly can

be made to beat again This accident may occur during operations as a result of the toxic effect of the anesthetic hemorrhage or cardiac trauma or it may be produced reflexly by careless handling of the abdominal viscera

Defibrillation of the ventricles has been accomplished by Beck His method is described on page 474 If ventricular standstill is present intra cardiac injection of epinephrine may be successful (page 475)

In emergencies when efficient cardiac contractions suddenly cease the first thought should be to maintain the blood supply to the vital cerebral structures Oxygen should be given through a face mask and direct cardiac massage begun to prevent irreparable damage in the brain areas while measures for restoring normal cardiac contractions are being instituted

## ACUTE CORONARY OCCLUSION

### Symptoms and Signs

1 **Pain** Usually lasts an hour or more but in rare cases it may be absent An attack of paroxysmal dyspnea or cardiac asthma may be the presenting symptom of the occlusion
2 **Shock** Patient usually cold, pale, sweating with rapid, thready pulse and low blood pressure In small occlusions shock symptoms may be very few or absent altogether
3 **Fever** leukocytosis friction rub, acceleration of the sedimentation time are LATER SIGNS

### Treatment

Rule If the patient presents the textbook picture, the diagnosis is easy If in doubt, be cautious and prove the absence of occlusion before allowing the patient to be up and about

1 **Bed Rest**
2 **Morphine for Pain** Give enough to control the pain satisfactorily usually 0 016 Gm (¼ grain) at first dose and repeat in half hour if necessary and every two or three hours thereafter as required Respiratory rate is guide to dosage Nitroglycerine is useless
3 **Oxygen** A great advantage if available Use nasal catheter method in the home (page 99) A tent (page 101) is the method of choice in the hospital Oxygen should be continued until the pain disappears and the cyanosis is absent
4 **Digitalis is Contraindicated in Acute Coronary Occlusion Unless Symptoms of Cardiac Failure are Precipitated by the Accident** Digitalis may cause an attack of ventricular fibrillation Quinidine has been recommended for routine administration to prevent this complication (page 274)
5 **Glucose Is of Value** It increases available glycogen and provides food for the distressed myocardium Give 50 cc of 50 per cent solution very slowly into the vein using a 50 cc syringe in an emergency
6 **For Shock** caffein sodium benzoate 0 5 Gm (7½ grains) hypodermically

## HEART FAILURE

### I Congestive Type
(page 73)

#### SYMPTOMS

Dyspnea progressing to orthopnea Edema Large liver Rales in the chest Increased venous pressure Any arrhythmia may be associated with congestive failure

#### TREATMENT
(page 74)

1 **Bed Rest**
2 **Morphine** 016 Gm (¼ grain) third hour as required
3 Obtain an experienced attendant at home or send the patient to the hospital
4 **Restrict Fluids**
5 **Digitalization** (page 75)
6 **Mercurial diuretics** (page 88)
7 **Oxygen** (page 98)

### II Paroxysmal Cardiac Dyspnea or Cardiac Asthma
(Acute left ventricular failure)

#### SYMPTOMS

Those of advanced heart disease Sudden attacks of dyspnea occur usually at night and may progress to orthopnea The lungs quickly fill with rales Later edema occurs Death may follow in the absence of prompt treatment

#### TREATMENT

1 **Morphine** 15 mg (¼ grain) by hypodermic immediately
2 **Venesection** 400 to 600 cc (Indications cyanosis distended jugular veins and dyspnea)
3 **Oxygen** if available Nasal catheter method at home Tent if the patient is in the hospital
4 **Aminophyllin** 0 24 Gm (3 to 4 grains) intravenously
5 If attacks recur frequently mercurial diuretics may be valuable in lessening the incidence in some cases

## THE PAROXYSMAL TACHYCARDIAS

### Auricular

Heart rate is 160 to 200
Onset sudden Offset sudden

#### SYMPTOMS

**Palpitation**
**Vertigo**
**Syncope (rare)**

#### DURATION

Few minutes to few hours
*Very rarely paroxysms continue over a week*

#### CAUSE

None may be present
Heart usually normal
Heart disease may be present (most common type rheumatic)

#### TREATMENT

Try in order
- **Carotid sinus pressure** (page 379)
- **Vagal stimulation**
  - **Eye ball pressure**
  - **Tickle throat to cause gagging**
  - **Emetic (ipecac)**
- **Quinidine** (page 383)
- **Mecholyl (?)**

### Ventricular

Heart rate rapid (120 to 160) regular At times may be irregular

#### SYMPTOMS

Onset abrupt Premature beats occur before seizure occasionally in runs of two or three Often these may be recognized and act as a warning
Heart disease present usually serious Commonly coronary occlusion

#### TREATMENT

**Quinidine**
**Carotid pressure *ineffectual***
**Digitalis dangerous**

## AURICULAR FLUTTER

1 Heart rate 100 to 150 It may change
2 Onset is sudden
3 The termination may be gradual or sudden
4 Heart disease is usually present
5 Carotid sinus pressure often slows the ventricular rate

### Treatment

Digitalize This changes flutter to fibrillation Withdrawal of the digitalis may then cause the rhythm to return to normal If advanced heart disease is present a maintenance dose of digitalis should be continued (page 394)

Quinidine has been used to stop paroxysms if no heart disease is present or cardiac damage is slight Digitalis however is the drug of choice

## AURICULAR FIBRILLATION

1 Heart rate 100 to 160
2 Rhythm Irregular EXERCISE INCREASES THE IRREGULARITY
3 Heart disease
   Almost always present
   In rare instances the heart may be normal
4 The onset is sudden
5 Termination may be abrupt

### Treatment

Digitalize if heart disease is present (page 395) A good response to the drug may be predicted In instances in which fibrillation is paroxysmal and heart damage is slight quinidine is indicated

## ADAMS STOKES SEIZURES

### Symptoms

Syncope Convulsive movements No paralysis Evidence of arteriosclerosis is apt to be present and the patient is usually beyond middle life There may be a previous history of seizures The pulse is slow (10 to 30 per minute) or the patient may be pulseless Recovery occurs in a few minutes to five minutes Death may occur in any of the seizures

### Mechanism

There may be a cardiac standstill or prefibrillary type of ventricular tachycardia with short runs of ventricular fibrillation These cause cerebral anemia

### Heart Disease

This is present usually with partial A V block alternating with periods of complete A V block Normal sinus rhythm is seen in rare cases The heart block usually follows a gradual or acute occlusion of a coronary artery Other causes of heart block (gumma tumor, endocarditis etc ) are rare

### Treatment

Usually unsatisfactory at the time of the seizure If electrocardiographic proof of cardiac standstill has been obtained intracardiac injection of epinephrine may be given (page 475) Use 0 5 cc of a 1–1000 solution In an extreme emergency do not wait to boil up equipment Use lumbar puncture needle and 2 cc syringe Limit use of intracardiac injections to this type of emergency and cases of sudden cardiac standstill during anesthesia

### Follow up Advice

Bed rest until a complete cardiac study is obtained To prevent recurrence of attacks many drugs have been recommended These include ephedrine benzedrine thyroid extract, metrazol and barium chloride (page 403)

## EMBOLISM

### Mechanism

**Detached thrombi** (1) from auricles in cases of mitral stenosis or subacute bacterial endocarditis and from ventricles in cases of coronary occlusion or subacute bacterial endocarditis (2) from pelvic or thigh veins on tenth to fourteenth postoperative day Emboli go to lungs or systemic vessels depending on the point of origin From right heart destination is lung except in rare instances where there is a patent foramen ovale Air or fat emboli follow trauma

### Symptoms

If embolus lodges in extremity there is first PAIN followed in a few hours by pallor and drop in temperature on affected side No arterial pulsation is present below the point of occlusion

### Treatment

1 Morphine for pain
2 Keep the patient warm and combat shock The extremity should be wrapped in cotton
3 Oxygen for pulmonary embolism in presence of cyanosis and dyspnea (page 98)
4 Consider embolectomy if the site is known and the vessel can be quickly reached by the surgeon If gangrene present amputation
5 **Avoid massage**

### Preventive Measures

These are important postoperatively in the prevention of pulmonary embolism (acute cor pulmonale)
1 Trendelenburg position
2 Carbon dioxide administration several times daily during the first 48 hours
3 Frequent deep breathing exercises
4 Keep extremities warm both during and after operation
5 Massage and passive motion of legs during the first 48 hours after operation
6 Thyroid gland (U S P ) may speed venous return and is useful in carefully selected cases

## PERICARDIAL EFFUSION

### Etiology

Pneumonia In this disease the effusion is apt to become purulent (page 171)
Tuberculosis Large effusions often occur (page 177)
Rheumatic fever Large effusions are rare but can occur (page 162)
Malignancy Large effusions rare

### Signs

Friction rub
Fever
If fluid accumulates in amounts above 300 cc, signs of compression of the heart may develop The onset of symptoms may be sudden dyspnea, cyanosis increased venous pressure and fall in pulse pressure (page 164)

### Treatment

Pericardial paracentesis For technic see page 166
Surgical drainage if effusion purulent (page 174)
Sodium cacodylate intravenously in daily doses of 5 to 8 grains (Willius)

## WOUNDS OF THE HEART

### Signs

Shock with evidence of puncture wound of the chest in cardiac area Falling blood pressure increase in venous pressure and other signs (if patient survives) of acute cardiac tamponade

### Treatment

Immediate operation If knife or foreign body still in the wound do not remove it until the field is exposed and suture can be carried out (page 494)

## PERIPHERAL CIRCULATORY FAILURE
### (SHOCK, COLLAPSE)

### CAUSES

1 Diminished blood volume with a subsequent decrease in the cardiac output following
   Hemorrhage
   Trauma with leakage of fluid into tissues of the injured area thus decreasing venous return
   Diarrhea
   Vomiting
2 Increase in the vascular bed (?) resulting from the action of toxins (vasodilators) in pneumonia typhoid etc
3 Neurogenic This type has more acute onset and is usually less serious It is caused by decrease in the vascular tone and reflex cardiac inhibition (vagus)

### SYMPTOMS

1 Patient apathetic
2 Pallor (blood lost or pooled in other areas)
3 Eyeballs sunken features pinched (fluid loss)
4 Temperature subnormal The extremities are cold
5 Low blood pressure (80/60)
6 Pulse is weak and rapid
7 Heart sounds are weak
8 Respirations are slow

### TREATMENT

**Depends on factors operative in each case**

1 Keep the patient warm The head should be low
2 Give enough morphine to prevent restlessness and relieve pain
3 Transfusion using hypertonic or colloidal solutions Blood is ideal As a substitute use two to four per cent saline or five to ten per cent glucose Acacia has been recommended
4 Drugs of vasoconstrictor group useful in neurogenic shock
   a Epinephrine hydrochloride One cc of 1 1000 solution (subcutaneously)
   b Ephedrine hydrochloride can be given by mouth in doses of 0 045 Gm (3/4 grain)
   c Pituitrin (surgical) one cc (subcutaneously)
   d Caffein with sodium benzoate (U S P XI) given subcutaneously in 8 grain doses is occasionally of value

**Note** Digitalis is contraindicated and should never be used since the rapid heart rate is compensatory owing to the diminution of the blood volume

# 19

# PHYSIOTHERAPY IN THE TREATMENT OF HEART DISEASE

It is part of the cure to wish to be cured —SENECA, *Hippolytus* 1, 249

The use of physiotherapy in the treatment of cardiac patients is not a new concept In the days of Hippocrates physicians were skilled in these measures, and the location of the temples showed their regard for the healing powers of Nature The ancient Celts and Romans recognized the virtues of the mineral springs and advocated hydrotherapy Many Roman coins and other objects which support this belief have been found in the springs at Bad Nauheim Spas were fashionable in Smollett's England and the sharp sighted Matthew Bramble in Humphrey Clinker gives a vivid summary of his opinion of the resorts of his time, All these places have their vogue and then fashion changes" This remark is equally true at the present time although the Matthew Brambles of our day do not suffer from rheumatism and do not travel in coaches Coronary disease has become a more common affliction in an age when the transport plane replaces the coach

The physiotherapeutic measures that have been recommended in the treatment of cardiovascular disease are many and varied, but are either little known or infrequently made use of by the general practitioner Smollett's remark I have neither time nor opportunity to confirm by experiments the particular notions I entertain concerning the efficacy of these waters—[347] can be applied equally well to his professional brethren almost 200 years later This is unfortunate since the chronic sufferer from heart disease often believes his problems are being inadequately managed when something active is not being done for him and many types of cardiac patients turn to the cults where activities of all forms thermal electric and manual are much in evidence The patient consequently passes out of the hands of the physician who possesses a knowledge of the etiology functional capacity and treatment of heart disease to be taken care of by the member of a cult who usually does not know the indications or contraindications for the various methods he employs

The limited training in physiotherapy that the modern physician receives while in medical school probably accounts for the lack of facilities in most hospitals and communities throughout the country The average physician does not know when and to what extent he should take advantage of physiotherapeutic methods in the treatment of chronic disease However, even if he is alert in this respect, there are today few places in

our country where he can send patients with small incomes The resorts and the elaborate establishments are still luxuries that most patients can not afford It remains for the local or state authorities to provide suitable sanatoria where patients of limited means can receive such treatment Perhaps then physicians interested in this work may have time to confirm by experiments prevailing opinions on this form of therapy

## SPA TREATMENT

The spa treatment provides physiotherapy with diet and rest and this accounts largely for its success It is this combination of the spa and its mineral springs with their endless supply of naturally charged water that attracts the patient for it is doubtful if physiotherapy in itself has much appeal to the average patient Consequently we should consider at the start the location organization and equipment of the spa This knowledge of the modern health resort should be familiar to every physician who allows his cardiac patients to undertake the journey seeking the cure for the best results are obtained when the indications and contraindications for this form of therapy are kept in mind

There is a time during the course of treatment of every cardiac patient who is either convalescing from an attack of congestive failure or approaching the end of a rest period following a coronary occlusion, when surroundings become irksome routine medicines sicken and dissatisfaction with life the family and local doctor becomes quite evident Every physician recognizes this phenomenon His patient is not ready to resume his customary duties but is able to increase his activities and venture beyond the confines of the bedroom for the first time The very chronicity of the cardiac ailment and the chorus of don ts from family and doctor discourage the patient and make him yearn for a change At this point in the management if finances permit properly supervised spa treatment may prove very helpful

The spa is the Shangri La of the modern business man He enters upon a new regime of treatment with enthusiasm and life takes on a rosy glow He is removed at once from daily contact with motor noises exhaust gases traffic snarls jangling telephones city apartments radio loud speakers night clubs and well wishing friends and he enters upon a period of training at the spa where something is being done for him every minute of the day Attendants hop bands play and it is small wonder that his lagging spirits rise The initial circulatory stimulant is purely psychic but none the less beneficial The patient meets other sufferers from similar ailments and in their company he willingly follows the plan of treatment devoted to cardiac preservation In this cheerful setting where nothing is lacking to provide comfort and happiness he is taught to live within the limits of his reserve If the spa cannot cure, it can educate and IT IS JUST AS IMPORTANT TO TRAIN THE CARDIAC PATIENT IN HABITS OF LIVING AS IT IS TO TRAIN THE DIABETIC IN HABITS OF EATING

The success of physiotherapy at the spa depends a great deal on the proper selection of cases At the beginning of the present century Mackenzie in plain language pointed to the folly of physicians who allowed cardiac cripples totally unfit for travel to undertake long journeys to the spa for the cure He coined the term 'Nauheim wrecks for patients who returned much the worse for the experience The physiotherapeutic measures used at the spa are most beneficial in ambulatory cases from Therapeutic Classes A B and C In other words, patients with evidence of congestive cardiac failure severe cardiac asthma angina on slight exertion recent or large occlusions advanced syphilitic heart disease subacute bacterial endocarditis and active rheumatic carditis do better at home under the care of the family physician Patients who have mild angina obesity hypertension and effort syndrome as well as sufferers from peripheral vascular disorders particularly of the spastic type the coronary occlusion convalescents and patients with inactive rheumatic disease and diminished cardiac reserve may derive some benefit from a course of Spa treatment

From the description so far it is evident that much of the cure depends on the environment and the attendants and may be classed as psychic Consequently in the following attempt to sum up the benefits of the different forms of therapy we must admit that there are many advantages that cannot be measured by the yardstick of science

## HYDROTHERAPY

Hydrotherapy (Balneotherapy) is usually administered as a carbon-dioxide bath This form of therapy in cardiovascular disease was originated at Bad Nauheim in Germany and such favorable results have been reported that other centers have been established where naturally carbonated waters are available in large quantities Well known spas are located at Bath and Harrowgate in England Royat and Vichy in France Bad Nauheim in Germany and Saratoga Springs Bedford Springs, Hot Springs White Sulphur Springs and Palm Springs in America

**The carbon dioxide bath** is prepared from mineral waters which emanate from the earth When this water reaches the surface great quantities of carbon dioxide escape but the bath retains a high percentage of the gas in solution a fact that can readily be demonstrated by observing the large amount of carbon-dioxide bubbles that cling to the body surface of the patient immersed in the bath (Fig 160) The amount of carbon dioxide in the water as it comes from the earth averages 0 7 to 1 4 Gm per liter although it is higher at some spas Different springs at the same spa sometimes vary in their carbon-dioxide content The water from these springs is always alkaline in reaction

The temperature of the water as it issues from the earth should not be too high in order that enough carbon dioxide may be retained in solution The ideal temperature has been found to be between 97° and 99° Fahren

heit However many resorts such as Royat have springs of varying temperature permitting a wide choice in prescribing a natural bath to suit the needs of the individual patient

The effect of hydrotherapy on the cardiac patient has recently been studied by a number of observers[10, 11] The mechanical effect of the bath itself the temperature at which it is given and the chemical effects of the carbon dioxide on the bodily processes locally and after absorption, are the main facts to be considered in an evaluation of this form of therapy

It is a common observation that the skin of the patient in the carbon dioxide bath becomes hyperemic up to the level of immersion This is at



Fig 160 Bubbles of natural carbonic acid gas blanket the whole body in the baths (Courtesy Dr Walter S McClellan Saratoga Springs New York)

tributed by some to the direct vasodilating action of the carbon dioxide on the skin vessels Consequently during the first few minutes in the bath the patient experiences a pleasing sensation of warmth even if the temperature of the water is below 99° F and an immediate effect is reflected in the blood pressure A gradual drop in the systolic as well as the diastolic levels occurs the peak is reached in about ten minutes In some patients a 30 to 40 mm decrease in the systolic blood pressure is not unusual If the patient stays in the bath the pressure will be observed to rise again and will reach its initial level in about ten minutes It is claimed that as the number of baths increases there is a tendency for the pressure to remain at lower levels in certain groups of patients and this is accompanied by an increase in the oscillometric index However we must always be careful in interpreting results in terms of the blood pressure reading that is so easily influenced by a variety of psychic factors The blood pressure would naturally tend to decrease in some cases in the atmosphere of the spa amid the pleasant surroundings and in the absence of disturbing contacts

During immersion in the bath the pulse rate drops and according to

some observers an actual diminution in cardiac size may follow the treatment

The pressure of the water of the bath may likewise aid in venous emptying Intra abdominal pressure may be increased by the weight of the water and this may augment the volume of venous blood returned to the right side of the heart Kroetz and Wachter have shown that in the baths at Nauheim *there is an increase in the minute volume output of the heart* The increase is greater in the carbon-dioxide bath than in the plain or fresh water baths It is also claimed that the respiratory center is stimulated directly by the increased amount of carbon dioxide in the arterial blood during the carbon-dioxide bath This may be caused by the increased amount of the gas absorbed from the skin and eliminated through the lungs or carbon dioxide may be inhaled from the environment In any event the amount of carbon dioxide eliminated by the lungs during and following the bath increases [61] Moreover the oxygen consumption appears to be only slightly greater certainly not to the extent that would indicate that the carbon dioxide comes from the oxidative changes of metabolism

In spite of these studies the exact mechanism of the action of the carbon dioxide remains unsettled The observers who support the theory of local action claim that the whole effect of the bath results from the stimulation of the cutaneous nerve endings Marked vasodilatation occurs the reflexe cause slower heart action The repetition of the baths accounts for the good effect in certain spastic arterial diseases of the extremities The proponents of the absorption theory claim that the gas enters the body in solution and acts on the organism as a whole increasing respiration by action on the respiratory center in the medulla The excess carbon dioxide in the mineral water causes peripheral dilatation and this again allows more carbon dioxide to pass through the skin Some observers carry the theory a step further They claim that the carbon dioxide acts as a sedative for vagosympathetic excitability and that it stimulates nutrition by improving the basal metabolism and helping in the excretion of toxic products In their opinion this explains the beneficial effect in hypertension A diuretic action has been said to be another good effect brought about by the carbon dioxide bath *through its increase in the basal metabolic rate*

The improvement in the morale may explain the good results that follow spa treatment in many of the coronary cases particularly in the patients who have mild degrees of angina Many angina cases especially if hypertension is present are apt to show periods of temporary improvement under any new forms of therapy A study of the electrocardiogram before and after the usual regime of spa treatment in 107 cases is offered as evidence of improvement by Comstock and his associates [70] However it must be realized that in no condition is the electrocardiogram subject to so much variation as in coronary disease particularly in patients recovering from minor occlusions

Considering the various effects of the carbon-dioxide baths that I have outlined, both real and theoretical the first indication for this type of treat

ment seems to be certain forms of hypertension where the secondary changes have not been too widespread or rapid but where the symptoms have been persistent and annoying Whether or not we believe the claims made for carbon dioxide baths any therapy that proves useful in calming the dangerous crises encountered in the hypertensive group and allows periods of relief to punctuate the course of a disease acknowledged to be chronic should be used even though we cannot analyze every phase of its action I do not believe that the effect of the carbon-dioxide baths is at all lasting in the majority of cases of established essential hypertension but I do believe that their use combined with other measures at the spa is far better treatment for this group of patients than any other system of therapy in the absence of symptoms of cardiac failure

While it is unfortunate that the result of the carbon-dioxide baths is regarded in terms of so many millimeters of fall in the blood pressure by both patient and physician on the other hand observations of the blood pressure are a great advantage in selecting cases The patients who show a moderate drop in blood pressure accompanied by a feeling of well being after the first carbon dioxide bath are usually the ones who will show the most benefit from a series of these treatments If the blood pressure seeks its former level when the patient returns home however he should not be discouraged for this does not indicate that the stay at the spa has been in vain If the onward march to ultimate cardiac failure has been at all de layed by the rest program that accompanies the treatment much can be said in favor of the spa Likewise if the cardiac patient returns from the spa with his mode of living adjusted to a more moderate level he should not worry about his blood pressure readings He should realize that many of his annoying disturbances such as vertigo headaches and flushes have been at least temporarily benefited by the treatment

The spa regime should prove of great value to the obese hypertensive who has the ruddy glow of health since it combines dietary regulation with hydrotherapy and the proper prescription of exercise Careful atten tion to every detail often makes it possible for the spa physician to un cover and treat successfully some secondary condition this in the long run reacts favorably on the hypertension The thin hypertensive patient who is subject to vascular spasms obtains relief because of quiet environ ment and the dilating effect of the carbon dioxide baths Much benefit likewise results in all groups of patients when they learn that they can live without having blood pressure readings taken several times a day

I heartily disagree with the claim that reduction of the blood pressure in the presence of aortic insufficiency is a benefit to be derived from the $CO_2$ cure This form of hypertension is a compensatory mechanism and in itself is certainly no indication for therapy Likewise the hypertension associated with an advanced renal lesion and early renal decompensation is not the type that is amenable to vigorous spa treatment When carbon dioxide baths are said to have ameliorated the renal lesion eliminating the albuminuria and decreasing the blood pressure level and nitrogen re

tention I always wonder what the patient's course would have been without the special therapy, since renal lesions many times display quiescent periods

The sedative action of the carbon dioxide baths may be counted on to help patients with overactive sympathetic nervous systems particularly those who show little if any basic cardiac damage and who are constantly plagued by frequent premature beats The same may be said of patients suffering from frequent paroxysms of tachycardia where the usual drug therapy is either poorly tolerated or ineffective in preventing recurrence of the seizures Patients with the tachycardia of mild hyperthyroidism may take the cure if financially able Surgery however offers the poorer patient a much quicker return to health Physiotherapy is contraindicated in advanced hyperthyroid states with cardiac signs and symptoms However during convalescence following surgical treatment physiotherapy may be useful

To give the reader an idea of the number temperature and types of baths administered the following case histories from a recent article by McClellan [44]* showing the course of hydrotherapeutic treatment advised in each instance at Saratoga Springs are included

## ILLUSTRATIVE CASES

**Case 106** H M male age 75 was referred by his physician to Saratoga on April 9 1935 Some dyspnea on moderate exertion and claudication in the lower extremities on walking short distances were present for some years

PHYSICAL EXAMINATION The patient was above the average height thin and distinctly nervous It was difficult for him to sit still during the examination There was arcus senilis and slight pulsation of the larger vessels of the neck His heart was slightly enlarged to percussion and the pulse rate was 95 There were numerous premature beats occurring at irregular intervals The blood pressure was 152 systolic and 90 diastolic The radial arteries were palpable and not easily compressed The lungs were clear Abdominal examination was essentially negative In the extremities the reflexes were present and weak pulsations could be detected in both dorsalis pedis arteries There was slight pitting edema about the ankles

CLINICAL DIAGNOSIS A Etiologic *Arteriosclerosis* B Anatomic Cardiac enlargement C Physiologic Premature ventricular contractions D Functional Classification Class 3

COURSE OF TREATMENT The following table presents in detail the temperature duration and position of the patient in the bath as well as a record of his pulse before during and after each bath

| | Bath Prescription | | | Pulse | | |
|---|---|---|---|---|---|---|
| Date | Temperature F° | Duration Minutes | Full 3/4 or 1/2 Bath | Before | During | After |
| April | | | | | | |
| 9 | 95 | 8 | 3 | 90 | 88 | 85 |
| 10 | 95 | 9 | | 85 | 84 | 83 |
| 12 | 95 | 10 | | 85 | 87 | 80 |
| 13 | 94 | 10 | | 84 | 92 | 80 |
| 15 | 94 | 10 | | 84 | 91 | 78 |
| 16 | 94 | 10 | | 85 | 80 | 78 |
| 17 | 94 | 10 | | 83 | 79 | 76 |

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| | Bath Prescription | | | Pulse | | |
|---|---|---|---|---|---|---|
| Date | Temperature F° | Duration Minutes | Full ¾ or ½ Bath | Before | During | After |
| April | | | | | | |
| 22 | 94 | 10 | Full | 73 | 78 | 78 |
| 23 | 94 | 10 | | 77 | 77 | 78 |
| 24 | 94 | 11 | | 78 | 76 | 77 |
| 26 | 94 | 12 | | 77 | 76 | 77 |
| 27 | 94 | 12 | | 78 | 77 | 76 |
| 29 | 94 | 12 | | 78 | 76 | 75 |
| 30 | 94 | 12 | | 79 | 75 | 74 |
| May | | | | | | |
| 2 | 94 | 12 | | 78 | 74 | 78 |
| 3 | 93 | 12 | | 78 | 75 | 77 |
| 4 | 93 | 12 | | 8 | 74 | 76 |
| 6 | 93 | 12 | | 7[illegible] | 75 | 74 |
| 7 | 93 | 12 | | 76 | 74 | 75 |
| 9 | 93 | 12 | | 75 | 74 | |
| 10 | 93 | 12 | | 74 | 73 | 76 |

Progress Notes April sixteenth The patient while still nervous has less edema about the ankles He states that pain in the legs is less severe The heart rate is 85 and frequent premature beats are still present

April 23 Symptomatic improvement is evident and the patient states that he can walk with less dyspnea and pain than at the beginning of his treatment

May Th re is still very slight edema at the ankles The pulse rate is 78 with the irregularity persistent

May 10 Pulse rate is 74 He states that he feels distinctly better There is no edema of the ankle although the cardiac irregularity still persists He is able to walk approximately one mile without the production of pain in the lower extremities

May 16 A letter from his physician written after his return states that both objectively and subjectively this patient is much improved and he is advised to repeat the course of treatment at the end of six months

**Discussion** This patient's history is typical of the gradual progress of a widespread arteriosclerosis The pain in the lower extremities was apparently an expression of diminished blood supply caused by the general arterial disease We do not expect that a patient of this type will show any decrease in the amount of arterial change or that the progress of the condition will be arrested The treatment however is of value in improving the circulation by making full use of the blood channels which are still available This type of patient does well on courses of treatment once or twice a year in order that the improvement noted above may be maintained The additional rest periods procured by visits to the spa likewise contribute in no small measure to the symptomatic relief obtained

**Case 107** R G male 46 was referred to Saratoga on July [illegible] 1935 by his physician who wrote that the man had been able to carry on his work in his usual manner until the past April when he had experienced a sudden sharp pain in the precordial region which had been sufficient to require bed rest The first attack of pain occurred in April 1935 and had been followed by a second attack on May 9 1935 The clinical examination and electrocardiographic tracings supported the diagnosis of coronary occlusion The physician stated that since the attack the patient had been at home and unable to perform any work although he had been up and about the house for the past six weeks not able to walk one or two blocks

The examination at Saratoga showed a well developed and well nourished middle

aged man Heart rate 78 regular both sounds distinct and no murmurs Blood pressure 13?/80

CLINICAL DIAGNOSIS A Etiological Arteriosclerosis B Anatomical Coronary sclerosis and old occlusions C Physiological Normal sinus rhythm D Functional Classification Class 3

TREATMENT The patient took the course of carbon dioxide mineral water baths shown in the following table

PROGRESS NOTES It will be noted that after the first bath there was an elevation in the rate of the pulse which may be accounted for by the nervous reaction following a new type of treatment

| DATE | BATH PRESCRIPTION TEMPERATURE F° | DURATION MINUTES | FULL ¾ OR ½ BATH | REST | PULSE BEFORE | AFTER |
|---|---|---|---|---|---|---|
| July | | | | | | |
| 22 | 93 | 8 | ¾ | 1 hr | 72 | 86 |
| 24 | 93 | 9 | | | 66 | 64 |
| 27 | 93 | 10 | | | 72 | 60 |
| 29 | 93 | 10 | | | 0 | 63 |
| 31 | 92 | 10 | | | 80 | 63 |
| August | | | | | | |
| 1 | 92 | 10 | Full | | 72 | 63 |
| 3 | 92 | 11 | | | 72 | 60 |
| 5 | 91 | 11 | | | 72 | 66 |
| 7 | 91 | 11 | | | 72 | 62 |
| 8 | 91 | 12 | | | 72 | 70 |
| 10 | 91 | 12 | | | 80 | 72 |
| 12 | 91 | 11 | | | 7? | 72 |
| 14 | 90 | 11 | | | 72 | 64 |
| 15 | 90 | 12 | | | 72 | 72 |
| 17 | 90 | 12 | | | 72 | 72 |

August 1 Patient states that he is able to walk five blocks without the production of any pain at the present time He is anxious to take up his work and it is difficult for him to follow a course of complete rest at home

August 17 The patient feels that he has distinctly gained in strength and is now doing light work around his home such as caring for the lawn and some l ght carpenter work His puls rate is steady at 7 good quality and his blood pressure i normal

DISCUSSION This patient undoubtedly had a good result following the period of spa treatment He is a typical example of the problem presented by the active business man convalescing from a coronary occlusion who experiences anginal attacks when first allowed to be out of bed The period of training the patient procured at the spa including the $CO_2$ baths was far more effectual in bringing about his return to work than drug therapy

There are additional features offered by the spa treatment that in my opinion far outweigh the value of the waters In this instance the spa was useful when placed between hospital and home At the spa this patient acquired the proper philosophy toward restricted living which an immediate return to the home and business would not have permitted He was given a good chance at the spa to become acquainted with his myocardial reserve and he did this with better grace when placed in the company of those similarly incapacitated The baths were prescribed but the routine rest periods that followed the treatments gave them their greatest value

Not the least of the benefits that some patients have shown following their visits to European Spas has been derived from the voyage over and back two enforced periods of physical and mental rest

## MASSAGE

Massage is another valuable measure that is commonly overlooked in the management of the cardiac patient The layman has always been awake to the value of this form of physiotherapy but as the physicians grew in scientific knowledge massage was unfortunately entrusted to others Continued neglect and lack of proper supervision gave opportunity for the rise of the various cults These less informed enthusiasts have gained in confidence and boldness until they claim to be able to cure almost any disease by massage

Massage has been shown to produce immediately dilatation of the capillaries the duration of which depends on the amount of pressure used [8] This effect can be observed by the direct inspection of the capillary bed with the miscroscope In addition the red blood-cell count is increased by forcing inactive cells into the circulation from resting areas Light massage can be useful even in cases of mild cardiac failure since it aids the return of venous blood and in long periods of inactivity makes up for the lack of the force supplied by contraction of the leg muscles Massage properly carried out therefore is an aid in preserving some degree of muscular tone and vigor

Massage is particularly valuable if given following the application of heat This principle is used in the Vichy douche where the entire skin area is sprayed by showers of different temperatures and then massaged After all these treatments whether local or general the cardiac patient should rest since the procedure is usually followed by a sense of fatigue In severe congestive failure with a high degree of venous engorgement massage is contraindicated It is likewise good policy to defer its use in the presence of fever acute endocarditis or acute myocarditis

## HELIOTHERAPY

Many of the spas have special rooms fitted with equipment for combining the effect of ultraviolet light with other forms of therapy In America the quartz lamp has invaded the hospital the athletic club the sanatorium the physician's office and lately the private home Much benefit is claimed from its use in various forms of heart disease including angina At present the subject is in a very unsettled state and further investigations are needed before definite conclusions can be made It may be a great aid in the treatment of children with rheumatic carditis (Fig 161) as we have long known that this disease flourishes in the crowded slum areas of the large cities where there is lack of sunlight and shows

decreasing incidence in the warmer climates of the South where the amount of sunlight is greater

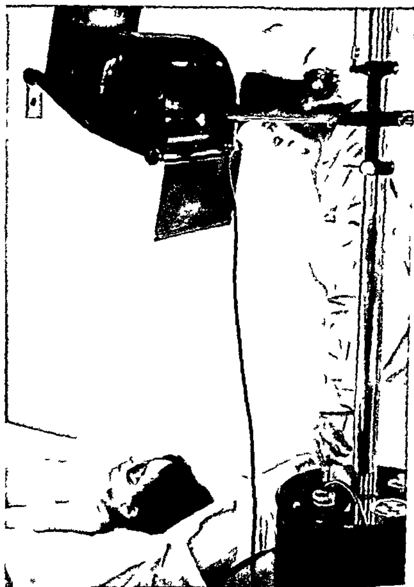


Fig 161 Heliotherapy (Courtesy Children's Heart Hospital Philadelphia)

## ELECTROTHERAPY

The value of the various electrotherapeutic procedures in the treatment of cardiovascular disease is still unsettled Further studies are essential to

support the claims that have been made for diathermy high frequency static sinusoidal galvanic and faradic currents Autocondensation and diathermy are most popular in the treatment of hypertension Diathermy undoubtedly has some place in the treatment of cardiovascular conditions where heat relieves the symptoms The greatest benefit follows its use in arterial diseases of the spastic type and intermittent claudication The treatments likewise have some temporary effect in relieving symptoms of other conditions In coronary disease accompanied by angina if the element of spasm predominates diathermy may be helpful by producing vasodilation and increasing coronary flow Some cases are reported where more lasting benefits have resulted than followed the use of the nitrite drugs In these instances the short wave diathermy has been thought to produce its good effect by a temporary paralysis of the sympathetic nerve pathways However in all these cases the psychic element is difficult to rule out

**Hyperpyrexia** The production of hyperthermia or hyperpyrexia by the use of the Kettering or similar apparatus has been followed by encouraging results in some cases of infection of the heart Cures have been reported occasionally in acute gonococcal endocarditis (page 189) and here the use of the method seems to be a rational one since it is quite possible to produce temperatures in the human body that the gonococcus cannot withstand

In chorea the use of the Kettering apparatus has many advantages Although great care should always be taken in the presence of an active carditis in recommending this form of therapy for children recent successes that have been reported are most encouraging It must be remembered that artificial fever is different from fever of toxic origin it is produced by electromagnetic induction and is not a fever in the ordinary sense but a heating of the body a hyperpyrexia Neymann [8] reports excellent results in a series of 25 cases of Sydenham s chorea In all cases the choreiform movements stopped following the treatments Similar results have since been reported by other investigators Neymann recommends that the treatments be given bi weekly, and that the temperature at each treatment should be maintained between 39 7° C (103 5° F) and 40 6° C (105 F) for eight hours After treatment the cardiac rate is increased and the T waves may be flattened but these changes disappear in 24 hours This form of therapy is not beneficial in all forms of chronic carditis and is not to be recommended for general use

## OCCUPATIONAL THERAPY

The proper form of occupational therapy can only be prescribed when a complete diagnosis of the patient is at hand and the functional classification determined consequently it is one of the final considerations in treatment Patients placed in Functional Group 4 can handle only the types of occupational therapy that can be carried out at bed rest Pa

tients convalescing from repeated attacks of congestive failure and the rheumatic groups with cardiac infection make up this category Although these cases are allowed very little exertion the mental rest that follows interest in some task that can be carried out for a few hours each day is a considerable aid to children and adults alike If improvement permits advancement to Group 3, and finally to Groups 2 and 1 the value of occupational therapy as a future means of earning a livelihood becomes important Some form of physiotherapy that is begun to interest the patient for a few hours a day may ultimately prove to be

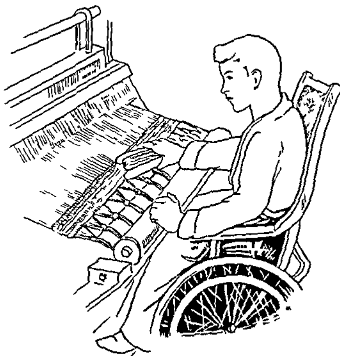


Fig 16 Occupational therapy

an excellent source of income Less financial worry often results and this is reflected in the health of the patient I recall an insurance salesman of *52 who came into the hospital on two occasions* following attacks of coronary occlusion He showed such limitation of cardiac reserve after the second attack that he was forced to give up his work He became much interested in the manufacture of sets of picture puzzles then at the height of their popularity When he left the hospital after two months he was improved but was still in Class 3 However he already had ideas for enlarging the business and with the help of his wife and daughter, who made up his sales force he was soon able almost to equal his former income This patient had an excellent outlook did not talk about his condition any more than it was necessary at the time of the visits of his

physician and never had time to realize that he was a chronic invalid He learned how to use his hands in a new occupation that allowed him to spare his heart Many other cases where the morale of the patient has been improved through the use of occupational therapy could be cited (chapter 23)

For Class 3 and 4 patients confined to bed various ingenious devices have been arranged to permit tasks requiring the use of the fingers only Light bed boards may be used or in some cases where weaving is carried out the apparatus can be suspended over the bed (Fig 162) Prolonged hospitalization permits training for occupations which require extensive apparatus while patients who come in for shorter periods may be assigned to simpler tasks like basketry cord and leather work Women patients may in addition to any of these types of occupational therapy renew their interest in different forms of needlework

Even in shorter illnesses the psychotherapeutic value of some slight task assigned cannot be overlooked The patient may be inclined to worry about his condition the new surroundings may delay his convalescence hence attempts should be made to interest him in some occupation as soon as his physical state permits In this way prolonged hospitalization may be prevented needed articles may be produced for the supply room (folded surgical dressings sponges etc ) and the patient s morale may be kept at a high level

# 20

# THE PRESCRIPTION OF EXERCISE

The wise for cure on exercise depend'
—DRYDEN, *Epistle to John Driden* 1 94

Exercise plays an important role in the management of the cardiac patient Unfortunately rest has been emphasized so much that patients are instinctively afraid of exercise, and for this reason physicians are apt to prescribe exercise cautiously and vaguely, if at all The prescription of exercise should present little difficulty if the physical examination has been made with care and the functional capacity determined The advice given to cardiac patients regarding their activities is based on this data as well as on the principles underlying the physiology of exercise

Energy for exercise is furnished by ingested food From a resting level when the requirements may be but one calorie per minute to the exercise level when the requirement may be ten times as great it can be seen that the resources of the body must be drawn upon to supply the energy as it is needed Analysis of the urine after the most severe exercise shows such a small amount of extra nitrogen that we know that the protein stores have been but little depleted Intelligently arranged training tables for athletes, therefore are not any longer overburdened with meat and other nitrogen containing foods, since the energy for muscular contraction is more quickly derived from the breakdown of substances that are non nitrogenous This is shown by a study of the oxygen absorbed and the carbon dioxide eliminated (respiratory quotient) The carbohydrates of the food furnish most of the motive power for muscular exertion Consequently athletes are now encouraged to eat candy before engaging in severe muscular activity

As a result of muscular contraction there is an accumulation of lactic acid which disappears rapidly in the presence of oxygen The chemical changes in the blood accompanying exercise are responsible for stimulation of the respiratory center There is likewise increase in the pulmonary blood flow proportional to the increase in ventilation, a rise in the output of the heart per minute and an accelerated heart rate The size of the heart of the normal athlete who is well trained is unchanged after severe exertion but the blood pressure shows a temporary increase This is more pronounced in the athlete because of the psychic factors of competition and is brought about by the constriction of the splanchnic area It permits widening of the capillary beds in the heart and skeletal muscles and aids in the quick diffusion of oxygen to essential areas

Although the presence of oxygen is not necessary for contraction of the

muscles it is most essential for their recovery A person can perform a given task without the necessary amount of oxygen being present for its full accomplishment For example he can hold his breath and climb a steep grade or lift a heavy weight but to do this the tissues go in debt for oxygen Our ability to proceed with the tasks requiring the sudden expenditure of energy without the appearance of symptoms depends upon this physiologic fact The debt of oxygen is paid back by a continued elevation of the respiratory rate following exertion for a longer or shorter recovery period until the balance is restored

The training of an athlete to accomplish a task with increasing efficiency and skill depends on daily practice This eliminates awkwardness and unnecessary movements and lessens the amount of oxygen needed each time The size of the skeletal muscles precipitating in the particular task is increased and the bodily processes of taking in the oxygen (respiration) and distribution of the oxygen (circulation) become better regulated and adapted The vital capacity increases as training progresses Consequently graded exercise may build up a reserve that enables the ultimate performance of a task to be accomplished with few if any distressing symptoms In a similar manner the cardiac patient can train his depleted reserve to perform more efficiently within narrower limits Therefore in neglecting to furnish the proper prescription of exercise the physician is not making use of all possible aids to recovery

Restriction of activity on inadequate grounds will consequently do more harm than overlooking a slight organic lesion and permitting full activity The mental effect of telling the patient that he has a heart murmur is tremendous particularly if it is followed by vague advice to take things easy for a while (chapter 13) A fear may develop toward all forms of activity and the subsequent lack of exercise soon reflects itself in a poor physical state Therefore it is most essential that the physician be fully acquainted with the physical condition of the patient before prescribing or prohibiting exercise

Let us consider first the types of heart disease where bed rest for prolonged periods is required In this group we include patients with congestive failure recent coronary occlusions and active cardiac infections Even in these instances active exercise in all forms is not contraindicated beyond a few weeks In exceptional cases even before this period has expired some forms of exercise may be definitely indicated to encourage the patient and keep up his morale Nurses trained in the care of cardiac patients are valuable at this time They help to take the patient's mind away from his condition and interest him in some form of exercise even if it consists only in moving the fingers in arranging cards or in making small articles Gentle massage may be started almost at once in many patients and this may be followed by passive movements If no ill effects are noted greater freedom may be allowed The Schott resistance exercises if properly carried out are often valuable in beginning the rehabilitation

When to allow the patient out of bed is a decision that rests on the facts of each case Experimental evidence demands that the rest period for the patient following an acute coronary occlusion should be not less than six weeks However, patients who show good recovery from congestive failure may be permitted to be out of bed much sooner When edema disappears and the appetite improves it is often good policy to allow a little freedom as early as the end of the first week It has been demonstrated many times that nothing is to be gained by unduly prolonged bed rest, particularly in cardiac patients at or beyond middle life Furthermore many complications are encouraged by an extended period of inactivity in elderly individuals

Walking is the next exercise that may be prescribed for this group the amount depending on the effect of the initial allowance on edema chest pain pulse, and respiration In the patient who has angina the increase in the exercise allowance should be gradual If chest pain is absent the prescription may be slowly and cautiously increased for it is likely that no harm is being done

The same rule governs the first time the convalescing cardiac patient goes down stairs or out-of-doors It is not harmful to descend a stairway for this in itself is a form of self administered resistance exercise and in addition may help to restore the sense of balance after a period of bed rest The return trip however should be taken slowly 'One step at a time is trite advice but it still holds

In prescribing the first walks outdoors tell the patient in definite terms how far he is to go The importance of graded walks at this stage of convalescence has long been recognized and is part of any well planned spa regime The most elaborate of the systems is the one proposed by Stokes and Oertel consisting of a series of carefully laid out walks the first covering a distance of 1/12 of a mile While walking this distance the patient lifts his weight up a 3 per cent grade If the response is good the grade is gradually increased and over the course of some weeks the patient will be able to cover a distance of two miles comfortably with the grade advanced to 15 per cent An elaborate course for this system of exercise was laid out some years ago at Hot Springs Arkansas Foot paths appropriately labelled by stone markers of varied hue lead the convalescent through scenes of natural beauty They are graded from almost level to very steep A truly American adaptation of the Oertel system may be found at Saratoga Springs where the patient takes his daily amount of prescribed walking through a carefully planned golf course

In obese patients this system of exercise is very valuable when combined with the proper dietary regime Over the course of eight weeks' treatment by diet and walks considerable improvement in exercise tolerance can be noted The more drastic forms of Swedish exercise carried out with the aid of gymnasium equipment, are less popular today but they are still useful when carefully prescribed The stationary bicycle and the rowing machine in the city gymnasiums and clubs furnish satisfactory forms

of indoor exercise for the winter months Intelligent supervision is much more important however than the type of exercise The response of the patient to each added burden is the essential factor for this suggests the amount to be added or subtracted from the next day s exercise prescription

Less fortunate patients who cannot take spa cures' may nevertheless derive benefits from walks if the physician will take the time to plan them Familiarity with the neighborhood of the patient s home or hospital will make this exercise prescription possible In addition to keeping alive the patient s interest in his treatment and progress the physician s notations concerning these exercise prescriptions show the functional capacity and when considered as a whole they are invaluable in estimating the effect of therapy as well as the ultimate prognosis in each case

Before planning suitable exercise for an ambulatory cardiac patient a knowledge of the occupation and temperament is essential I have never advised the so-called setting up exercises for they are tiresome in most instances and after the first few attempts are usually abandoned The ideal forms of exercise for cardiac patients are the intermittent and non competitive types Golf for example is excellent if the patient s tastes run in this direction and a prescription of nine holes will be easy to accept This takes the patient outdoors away from business and adds the effect of heliotherapy for this reason it is far better than a gymnasium Furthermore if the patient is interested the golf is more apt to be continued Golf should not be attempted by those who are not interested in it or where competition cannot be avoided or if emotional strain is increased

The physician of today should have a fair knowledge of the different types of out of door activities if he is to prescribe these forms of exercise successfully Tennis and similar competitive games should not be allowed Croquet and other lawn games may be suitable as far as exercise goes but may be unfit as far as the personality of the patient is concerned Swimming if properly supervised is suitable in a number of cases The convalescing cardiac patient will usually prefer to take his allowance of exercise in the morning hours for then it does not interfere with sleep Wakeful nights are more apt to follow exercise periods taken at the end of the day

The ambulatory patient seen at the dispensary will have neither time nor money to follow any special program for exercise The question of exercise in these instances may be considered in relation to the usual type of work Cardiac patients are happier when permitted to return to work as soon as possible Exercise should be planned with this in view but before the schedule is made out the physician must have an understanding of the type and amount of exertion which the patient s daily work entails While lighter factory work may be permitted heavy laboring jobs are out of the question and here the great problem arises In days before the depression when opportunities for new positions were more plentiful the problem was usually settled satisfactorily by the Social

Service department (chapter 23) Today it is more difficult for the cardiac cripple to become self supporting but I have seen many patients who have demonstrated that it is not impossible Occupational therapy begun as a mild form of exercise and mental diversion may jump to the fore as a means of livelihood, since useful articles manufactured in convalescence may find a market later

As a general rule the cardiac patient with few exceptions should be encouraged to engage in some form of activity The complete retirement made possible by an insurance policy is not always a blessing and does not necessarily carry with it a guarantee of a longer life The attitude toward life that these patients sometimes adopt is by no means the best The lack of exercise is soon evident and if they are compared with the compensated cardiac patient of the same age with the same lesion who is physically fit, the difference is striking

In cases where the patient holds a more responsible position in the business world adjustment is much easier An earlier return to work may be permitted if a volunteer can be secured who will drive the patient to and from his office if this is at a distance With the question of transportation settled the hours of work can be adjusted according to the reaction It is better to start with a prescription of two hours and increase the working hours gradually Later with improvement short walks or the way to work may be added A few city squares in the early morning may lack the stimulating surroundings of the spa but after all it is the state of mind of the patient that influences the outcome of the battle This can be moulded and directed in large part by the physician during the early days of the illness

If the patient is of school age there are many questions to settle in regard to the exercise allowance when permission is given to return to classes Careful training of the cardiac child is possible so that the two extremes mentioned by Robinson[319] are avoided The child then neither attempts to cover up the handicap nor uses the handicap to 'cover up' The usual strenuous gymnasium activities should be entirely prohibited, but the milder exercises prescribed for correction of faulty posture may be tried for many times poor posture places an additional burden on the circulation The child should be encouraged to take walks The stairway of the school should not stand as a handicap to the education so essential to these cardiac children The steps can be taken if time enough is allowed The child who has a cardiac lesion should be taught not to run to school at school or after school

Upper respiratory infections are more serious in children because of the likelihood of stirring up a latent rheumatic infection For this reason all activities, including attendance at school, should not be permitted when fever is present It is always the best plan whenever possible to allow the child who is handicapped by a cardiac lesion to attend the special classes that have been organized in some cities for his care Here under the supervision of well trained teachers and in the company of other chil

dren suffering from similar limitations progress may be more satisfactory The children in these special groups or schools are taught to avoid haste in all things and a philosophy of living under a constant restriction of exercise is acquired Even when exercise has to be curtailed for long periods because of the recurrence of rheumatic infection education is still carried on in these special schools In this way the patient is prepared to fill a position in life that will not overtax a decreased cardiac reserve (page 131)

## THE HEART IN ATHLETICS

Nearly a century ago at the beginning of the modern era of collegiate athletics, James Hope in a book entitled Diseases of the Heart and Great Vessels expressed the opinion that boat racing at Oxford and Cambridge and violent gymnastics have caused

> rupture and inflammation of the aortic valves and aorta, issuing in incurable organic disease

He further stated

> I have also known pedestrian tours among the Swiss and Scotch mountains to be followed by hypertrophy and other diseases of the heart It is protracted efforts that are always most pernicious Feats of this kind should always be discouraged [181]

A similar stand was taken by Peacock in 1864 when he claimed that cardiac hypertrophy and subsequent failure among Cornish miners resulted solely from overwork In 1870 Clifford Allbutt claimed that long continued exertion caused right heart failure and dilatation and that sudden strains were productive of wear and tear in the aortic area In 1888 Roy and Adami s experimental work seemed to lend support to these claims and chronic thickening of the cardiac valves due to strain was described at length in their book Adami in 1911 stated that he believed the nodose arteritis seen in elderly subjects was associated with thickening of the valve leaflets both in his opinion resulted from mechanical strain In 1898 and 1909 Allbutt retrenched enough to admit that the influence of the toxic and infective factors was difficult to eliminate in these cases and sounded the first modern note in his conclusion that the importance of muscular effort as a factor in cardiac injury has been much exaggerated

However for years there were no dissenting opinions Reviewing the literature up to 1915 we find the old idea re echoed many times Bardeen[19] in 1915 stated

> All college students taking part in major sports have hypertrophied hearts While in many cases the compensation is good in a large number there is myocardial irritability sometimes accompanied by mitral murmurs which indicate somewhat serious lesions

For the past 25 years, with a few exceptions little attention has been given to the subject in American and English literature An extensive continental literature is available but it contains many conflicting opinions Consequently the subject of the heart and athletics remains rather hazy in the minds of many The prescription of exercise for damaged and undamaged hearts shows a surprising lack of uniformity in the various university centers and the functional systolic murmur continues to consign good athletes to the side lines In these cases even in the absence of hypertrophy or any supporting sign cardiac involvement is suspected, and even the mildest forms of exercise may be prescribed with hesitation and uncertainty

The sustained interest of both sexes in all forms of athletic activity places *the question of the heart in its relation to competitive sport* squarely before the health services of our universities Curiously enough the rising tide of interest in sports and their effect on the heart has been paralleled by revolutionary changes in our concepts of diseases of the circulatory system With Mackenzie and Lewis as leaders a newer cardiology has sprung up in which valve lesion and murmur are now relegated to the background and the heart muscle assumes major importance We have reached the time when the older idea especially the erroneous assumption that the athletic heart is a clinical entity must be discarded and our judgments must rest on the sounder foundations of these newer concepts

To begin with let us consider the normal heart of an athlete at the end of a hard race We look first at the clinical picture We see the runner gasping for breath we note his pale pinched expression and weak rapid pulse He perspires freely from a cold body If the exhaustion is more severe we may see him lying on his side occasionally doubled up complaining of abdominal pain There may be nausea even vomiting and sometimes unconsciousness Is this the picture that we describe as heart strain? If we pause and analyze the symptoms we find very little evidence that the circulatory system is at fault and we are forced to conclude that the term heart strain is a much misused expression When the term 'strain is used in connection with a skeletal muscle I understand a stretching or tearing of the muscle where it meets its tendon or of the tendon itself I can even visualize the rupture of a few strands of muscle with subsequent soreness and stiffness at the site but this same injury does not occur in the musculature of the heart Nature protects so vital a structure from injury that is so easily produced Moreover such an injury has never been seen postmortem in healthy hearts We do meet rare cases of rupture of the wall of the heart but rupture does not occur unless the area is the site of an infarct resulting from a previous coronary occlusion Authentic cases of spontaneous rupture of the healthy heart have never been reported Barth has collected 24 instances of spontaneous rupture of the heart and in every instance the seat of the lesion was in the left ventricle where the heart wall is usually the thickest So we

conclude that the rupture occurred through a degenerated most likely infarcted area

Likewise rupture of a healthy heart valve occurs rarely if ever and cannot be produced by severe exertion or 'strain' When it does occur the valve has been previously weakened by disease Take a section of healthy aorta with its semilunar valves in place and raise the pressure to the breaking point You will see the slender thin aortic valve leaflets hold fast while the thicker aortic wall will stretch split and then give way If similar experiments are tried upon the healthy mitral and tri cuspid valves the artificially increased pressure leads to stretching and regurgitation through the valve orifice rather than rupture of the tough valvular tissues We may safely conclude from this evidence that severe sudden exertion in the athlete will not produce strain or muscle injury to the heart such as we see in the skeletal muscles nor will it damage or rupture the valvular leaflets

Even the sudden death of an athlete at the finishing line (an extremely rare event) is not necessarily caused by the heart It may conceivably occur from an overlooked persistent thymus or may be brought about by the mechanism of vagal inhibition If the day is excessively warm and the race closely contested the possibility of heat stroke or exhaustion must be kept in mind May there not exist also, under these dramatic cir cumstances a condition closely akin to surgical shock? The psychic strain is certainly tremendous particularly in the much advertised stars before and during a hard race and is it not possible that the nervous system may be at fault and not the cardiovascular? Surgeons are notably heart conscious and in my experience they are inclined to blame on the heart all sudden deaths during or just after operations Here too the effect of the nervous system the ductless glands and other factors pro ducing shock are often overlooked The toxins of infection may leave in their wake not so much direct cardiac disability as a distinct loss of tone in the vasomotor system It is the latter condition that slows down the athlete Earlier exhaustion is noted many times in students when they have been permitted to resume activities too soon after recent infections like influenza

Acute cardiac dilatation is the most popular diagnosis advanced to account for symptoms observed in the athlete at the end of the race Indeed this diagnosis has enjoyed widespread popularity mainly be cause accurate methods of investigation have not been used Reports have been based on the percussion of the hearts of athletes a most unreliable method especially in heavy set well developed men Percussion usually gives a larger cardiac outline than the roentgen ray and this may be the main reason why the heart of the athlete has for many decades been wrongly suspected of showing hypertrophy caused by exercise Ortho diascopy is a better method to determine cardiac size of athletes and when carefully performed is cheaper and better suited to the need of a university health service

Immediate examination of the hearts of athletes with the roentgen ray as they fall exhausted over the finish line shows a heart shadow which is not that of acute cardiac dilatation in most instances the shadow is actually smaller than the normal Richards,[31] and later Gordon,[136] by a series of pictures on marathon runners showed that all hearts are smaller immediately after the race and return to normal size during the course of a day Experimental studies on animals which have been properly carried out and controlled seem to show a smaller heart when the point of exhaustion is reached So we must abandon the term acute cardiac dilatation when referring to the cause of exhaustion in athletes with normal hearts Even without the experimental proof which I have mentioned, the idea should appeal to us as being anatomically unsound The heart is limited in its power to dilate, especially if the process is acute by *the tough fibers of the pericardial sac If we perform Muller s experiment* under the fluoroscope we can see the heart dilate to the limit of its pericardial restraint and assume normal size as soon as the experiment is discontinued if healthy it is none the worse for the experience

The cause of the smaller heart size observed in the athlete after sudden exertion taxes our power of speculation The skeletal muscle, when subjected to overuse shows cramp and stiffness because of diminution in blood supply The overaction with the attending imperfect oxidation gives a swelling of the skeletal muscle fibers with tension of the sheaths Later there develops the painful stiffness so commonly met in those unaccustomed to exercise We cannot conceive of this phenomenon occurring in the healthy heart It is a vital organ necessary for the survival of the organism constantly beating with relatively short rest periods and with a more abundant circulation It is tempting to explain the smaller size of the healthy heart after severe exertion by an excess of lactic acid, but this has not been proved

Lewis [8] has come to the conclusion

> that the burdens imposed by physiological acts upon the normal heart however heavy these burdens may be never injure the heart fibers never produce injurious dilatation and never exhaust the heart s reserve

We must accept this explanation on the basis of experimental proof The heart of the normal athlete is an organ with a reserve far in excess of the organs and systems it supplies It cannot be strained because other bodily mechanisms have lower protective thresholds For example skeletal muscle cramp or cerebral anemia will set in and stop the athlete before the heart gives out Lately more knowledge of the effects of hypoglycemia has led us to attribute to that syndrome the condition of the athlete at the conclusion of the race The blood sugar levels of runners who are forced to drop out of marathon races is supporting evidence of this theory since on numerous occasions the blood sugar has been found almost to approach the level at which unconsciousness comes on

We must therefore take into consideration all these mechanisms before we blame the symptoms of dyspnea rapid pulse exhaustion or even coma on the heart Consider always the fact that Nature surrounds and protects the heart by a series of defensive barriers because it is so indispensable to life

One of the most discussed and interesting questions relating to the problem of the heart in athletics is the so called chronic enlargement supposedly resulting from strain long continued and referred to for years as athlete s heart" If we approach this problem by studying the hearts of lower animals and drawing conclusions from what we observe in them we may easily be misled Clark points out some striking differences in the heart weights in proportion to the body bulk of active and inactive animals and shows that dogs bred for speed have higher heart ratios than ordinary dogs Likewise Fox has shown that quiet birds like the owl have smaller heart ratios than active fliers This author also describes hypertrophy of the heart in captive mammals and birds, but he cautions us that the essential character of these changes is open to dispute in the absence of proof that some unrecognized previous infection or toxemia did not exist Since there are some striking differences in the physics of the circulation in the lower animals particularly in birds we must be on our guard and not draw general conclusions too readily However if work hypertrophy occurs among the commoner beasts of burden we should reasonably expect to find the pathologic museums of our veterinary schools crowded with these specimens Inquiry reveals that this is not the case

Studies by Gordon Richards and my own observations all show quite conclusively that enlargement of the heart of healthy athletes does not occur even when the period of training extends over many years Consequently we do not believe that participation in college athletics predisposes to cardiac enlargement and to the disability which commonly comes to those who have large hearts We cannot deny that the heart muscle develops the same as any other muscle and benefits from exercise which it needs whether healthy or diseased In consequence of this development there is it is true an increase in size but the amount of this increase relative to the initial bulk is small We know that the heart does not enlarge with exercise in the same ratio as skeletal muscle but even though we assume that it does the increase in size as we note it under the fluoroscope falls far short of the enlargement commonly seen as the result of disease We must admit at this stage of our discussion that concentric hypertrophy of the heart may be present and escape recognition under the fluoroscope but this form is rarely in evidence at postmortem

Gordon concludes from his careful study of marathon runners that many years of training and competition do no cause cardiac enlargement Pancoast likewise after examining the chest plates of many athletes found no cardiac enlargement in any of them He observes that among them was one of the world s greatest runners who showed no cardiac enlargement in spite of the fact that one lung was almost obliterated by pleural thick

ening and adhesions The examination of transcontinental foot runners who ran 3434 miles in 84 consecutive days, showed heart diameters within normal limits The only large hearts I have seen in athletes have been those secondary to previous unrecognized rheumatic infection

The relationship between active participation in school and college athletics and the early development of cardiovascular degenerative changes is another problem deserving attention The sudden death in middle life of a man who had previously been a world s record holder will be widely discussed and cited as an example of the ill effects of athletics on the cardiovascular system in later life Hundreds of others who engaged in the same form of training at the same university and who ran in the same races will be forgotten and their records uninvestigated Careful studies of athletes in later life are rare in the literature Morgan in his analysis of the first 24 Oxford and Cambridge boat races from 1829 to 1869 both in clusive in which he obtained information from all of the 255 living members of the crews except four showed that there is little appreciable difference in the mortality from heart disease among university oarsmen of corresponding age Edgecombe[87] also after careful inquiry into the histories of a large number of university oarsmen showed that they are no more short lived than nonathletic men nor are they prone to die of heart affections

The sustained interest in all forms of athletic activity in America should impress upon university officials the duty of providing the equipment necessary to carry out a complete study of the cardiovascular system of all athletes The usual methods of percussion a blood pressure reading and auscultation no longer suffice Fluoroscopy is needed to determine ac curately the cardiac size and shape Likewise routine electrocardiograms are indicated for those students who display any of the arrhythmias or who give a history of antecedent rheumatic infection

A special form for this study may be useful (Table XV) It should include a complete survey of the past medical and family histories We sometimes find the family history of great value when we are called upon to render a decision as to the advisability of a student engaging in athletic competition Should one or more members of the family show evidence of early cardiovascular degenerative changes we are apt to study the student more closely and to note in detail the response to exercise In this group special attention should be paid to any abnormal blood pressure elevations if long sustained The blood vessels of the eye grounds should be examined frequently for early changes

When the cardiovascular examination of each student is completed, the school physician should write a full opinion based on these findings The evidence should be weighed and the decision given and this should be done unhesitantly for uncertainty on the part of the examiner plays havoc with the mental condition of the student

Diseased hearts should be carefully and completely studied These stu dents should not be sent out with the cautiously imparted knowledge that

TABLE XX

FORM FOR STUDY OF ATHLETES

NAME
Address — Age — Date
Height
Weight

HISTORY
Previous general state of health
Has heart disease ever been diagnosed?
(When and by whom)
Colds — Scarlet fever
Tonsillitis — Diphtheria
Tonsils removed — Pneumonia
Chorea — Influenza
Growing pains — Recent loss of weight
Rheumatic fever — Operations
Thyroid disease — Other illnesses
Kidney disease
Athletic history — Sports indulged in
Endurance
Any family history of — Heart disease
Kidney disease
High blood pressure
Tuberculosis
General condition at present — Fatigue — Pain over heart — Shortness of breath
Palpitation

EXAMINATION
Type of individual — Build — Type of chest
Physique
Thyroid — Blood pressure — Pulse
Heart outline
Auscultatory findings
Electrocardiogram
Orthodiagram
DIAGNOSIS
Recommendations

they have heart trouble and should take it easy They need exercise and careful grading of their exercise They should be studied from the standpoint of the functional capacity of the cardiac muscle We cannot deny the fact that some forms of athletic activity have a definite value in the treatment of cardiovascular disease Furthermore in cardiac cases when compensation is good we may be gratified to observe some decrease in the heart size after participation in the graded exercises designed to fit their tolerance

A prescription of rest in the case of the student in whom the only finding is an apical or pulmonic systolic murmur is indeed radical advice He misses thereby much that college life offers the companionship of fellow athletes the sportsmanship that competition develops and the beneficial effects of sports in building his body for we cannot deny that properly regulated athletic training increases the efficiency of the heart assists the blood and lymph flow increases the vital capacity stimulates metabolic activity develops a higher resistance to bacterial invasion and if well regulated will act as a psychic diversion and improve the tone of the central nervous system If the student is denied these advantages on the

basis of a single incomplete (often only auscultatory) examination of the heart he will grow up with the belief that he is physically inferior Psychiatrists tell us that this may prove a serious blow to character formation The growing boy s whole attitude toward life may be adversely influenced to mention nothing of the possibilities of the effect of the lack of exercise on the tone of the cardiac and skeletal musculature

# 21

# DIET IN HEART DISEASE

I saw a few die of hunger of eating a hundred thousand
—BENJAMIN FRANKLIN *Poor Richard* 1736

Careful regulation of the diet is an important part of the management of the cardiac patient While dietotherapy occupies a foremost place when diabetes complicates cardiac disease proper attention must also be given to this aspect of therapy in the presence of obesity and hypertension The object of any dietary regime is to lessen the work placed upon the heart and when this is accomplished it will greatly aid the other forms of therapy in maintaining circulatory efficiency

Unfortunately the subject of dietetics is uninteresting to many physicians and as a result cultists have made extensive inroads in this important field The patient of today is interested in dietary matters and usually turns to the faddist only when he fails to get the necessary information on the subject from his medical adviser The obligation cannot be filled by having at hand printed sheets containing dietary instructions The patient is an individual and likes individual attention Consequently the value of any dietary scheme is greatly increased when it is written out for the patient at the time when treatment is discussed Moreover it is appreciated is talked about in the hinterlands and as a result is much more apt to be followed Before considering the detailed dietary management of the various types of heart disease the principles upon which these diets are constructed will be reviewed briefly

An adequate diet is made up of proteins fats carbohydrates salts water and vitamins It should have a caloric value sufficient to meet basal metabolic requirements plus the stimulating action of certain foodstuffs and the demands made by the type of work performed by the patient The average requirements for a man doing light work is 3000 calories per day while the average requirement for a woman is 2700 calories

Protein furnishes the material for the growth and repair of the body tissues and is an essential constituent of the diet While the adult does not require protein for growth it is still needed for tissue replacement All proteins consist of giant molecules that are split up during digestion into somewhat over twenty simple compounds that are known as amino acids These substances are further broken up into glucose and fatty acids Protein contains 16 per cent nitrogen, consequently each gram of nitrogen is equivalent to 6 25 Gm of protein metabolized The daily intake of protein should be about 1 Gm for each kilogram of body weight Man is a fortunate animal for in health adaptation is possible on diets that contain

a wide variation in the quantity of protein Inhabitants of the Arctic Circle for example may live indefinitely on a strictly carnivorous diet The cardiac patient should always use great care in the amount of protein foodstuffs that he selects While an amount sufficient to replace ordinary wear and tear should be allowed, amounts above 50 Gm a day may accelerate metabolism and cardiac rate and in this manner increase the work of the heart Consequently the specific dynamic action of this food stuff is a factor to be reckoned with at all times It is evident that over exertion after a meal rich in protein places a load on the myocardium that often has disastrous results The protein in the diet of the ambulatory cardiac patient should therefore be restricted and the amount may be as low as 0 5 Gm per kilogram of body weight

Carbohydrates are important constituents of the diet of the cardiac patient since they furnish the contracting heart muscle with its most readily assimilated food For this reason carbohydrates should make up well over 50 per cent of the energy content of the diet in patients who suffer from heart disease At the present time this is no burden to the poorer classes since nearly all carbohydrates are cheap and readily obtainable

Fats do not hold a place of importance on the menu of the cardiac patient In large amounts they exert a depressing effect on gastric secretion and slow the emptying of the stomach For this reason they should b used sparingly since all foods recommended to a patient who has advanced heart damage should be easily digested According to many writers, an excess of fat in the diet plays a part in the development of the generalized arteriosclerosis in diabetes nephritis and nephrosis The results of future experiments must be awaited however to prove the exact relationship of excess fat in the diet to degenerative changes in the presence of a normal metabolism

The mineral constituents of the diet are also important to patients who suffer from cardiovascular disease and may be obtained in the required amounts in milk and vegetables Sodium chloride is perhaps the only salt consumed as such and the regulation of its daily intake warrant consideration in the presence of congestive failure About 1 to 2 Gm of sodium chloride are needed daily but the average person consumes amounts far in excess of this figure

Calcium is essential, especially in children and unless the diet is carefully planned it is much more likely to show a deficiency of this element About 0 9 to 1 0 Gm of calcium is required daily and this can best be obtained in milk Approximately 12 mg of iron constitute the daily requirement although in pregnancy this figure is increased Iodine is essential to prevent the development of simple goiter and should be given in districts where there is a known deficiency This requirement may be met by the use of iodized salt

Patients on adequate diets usually obtain a sufficient supply of vitamins from the ordinary foods The green vegetables and fresh fruit juices supply

vitamin C, whole wheat bread and the preparations containing wheat germ furnish vitamin B whole milk meat fat and eggs add a plentiful supply of vitamins A and D The latter can be increased by the addition of cod liver oil The relationship between the vitamins and circulatory efficiency will be taken up in greater detail later (page 552)

## ANEMIA

Mild grades of secondary anemia have no demonstrable effect on the heart Severe secondary anemias and primary or Addison s anemia may produce fatty degenerative changes in the cardiac muscle High grades of anemia may contribute to the production of congestive failure in rare instances and anginal symptoms may arise from this alteration in the quality of the blood reaching the myocardium (page 423)

The heart disabled by anemia responds to liver therapy and a diet rich in substances that contain the anti anemic factors e g liver or its equivalent vitamins and soluble iron salts In anemia when achlorhydria is present gastrointestinal symptoms that are often productive of secondary cardiovascular effects may be prevented by suitable amounts of dilute hydrochloric acid taken with the meals

Weakness palpitation and tachycardia are other cardiac symptoms that often appear in patients who have severe anemias of the secondary type These may disappear when the cause of the anemia is discovered and treated

## ARTERIOSCLEROSIS

The relationship between diet and arteriosclerosis has been a favorite problem for investigators for many years Diets containing the various foodstuffs in different proportions as well as in excessive and insufficient amounts have been fed to laboratory animals Patients with disorders of metabolism have also been studied for some possible clue regarding the relationship of substances in the diet to the speeding up of the process of sclerosis

The results of animal experimentations have been interesting and suggestive but wide conclusions should not be drawn The feeding of meat to rabbits has been shown to result in considerable aortic sclerosis while rabbits on milk and egg diets develop extensive intimal sclerosis Cholesterol has the same effect according to some observers Others claim that the high protein diet causes the arterial changes that uniformly appear in these laboratory animals

Coronary sclerosis has also been noted in white mice following diets high in cholesterol Similar changes however have not been seen in dogs and other carnivorous animals We may surmise that the abnormal substances in the diets of the rabbits and mice produce deviations in metabolism and perhaps account for the arterial changes In any event we are driven

back to cholesterol metabolism and must admit that it differs in various species under the same conditions

In man we cannot say that excess intake of foods gives arteriosclerosis If obesity is directly related to hypertension (which I doubt), then it may influence in this manner the state of the arteries Undernutrition apparently does not lead to arteriosclerosis for if it did, this lesion would be a prevalent disease in many countries of the world today If high protein diets result eventually in arterial changes studies of Eskimos should show a marked evidence of arteriosclerosis This is not the case On the other hand races that exist mainly on carbohydrates exhibit abundant sclerosis so we cannot blame the high protein diets for degenerative arterial changes

Joslin s studies[176] seem to show that in diabetes the excess fat in the diet contributes to early sclerosis but here we must remember the metabolism is decidedly abnormal Neither can we blame the development of arteriosclerosis on diets that consist largely of alcoholic beverages for we do not find advanced changes in the vessels of alcoholics when viewed in the light of the age of the patient

It is a common observation that patients who have widespread arteriosclerosis accompanied by advanced changes in the coronary tree gradually lose weight This has been referred to as cardiac cachexia In some cases it may be accelerated by the effects of congestive failure on the digestive tract but it is seen also in patients who never show congestive phenomena Moreover, in the latter group, a marked loss of weight may occur when the appetite is good and when the intake of food is sufficient to meet the bodily requirements Beyond a doubt the arteriosclerotic changes interfere in some way with the proper absorption and utilization of foodstuffs These patients therefore, should be fed a rich full diet Large meals should not be allowed since the same result is obtainable through frequent feedings that have a small bulk but a relatively high food value

In this modern age we continually strive to make our treatment conform to the most recent opinions emanating from research laboratories The family physician of the old school in treating many members of the same family called the arteriosclerosis that developed at an early age in successive generations a diathesis If pressed in the matter of definition he would tell you "It s bred in them In these patients we should plan treatment not entirely along dietary lines but more toward the prevention of infection and the better regulation of damaging occupations if we hope to avoid early arterial changes The diet should of course be regulated in the presence of diabetes and obesity

In old age with the usual degree of arteriosclerotic changes present a slight weight loss of ten pounds or so should not in itself be cause for alarm While it has been truthfully said that the worst thing that can happen to an old man is to acquire a young wife who is a good cook most of the blame for the abnormal appetites of old people lies in the condition of their gastro-intestinal tracts possibly associated with unbalanced diets Abnormal sensations of hunger and capricious appetites

are common and are often associated with atrophic changes in the stomach and the secreting glands as well as atrophy of the usual reflex pathways While a diet complete in all the foodstuffs should be given to the older patient if there is demonstrable cardiac damage the amount of the food and the speed of its intake should be carefully guarded Circulatory accidents in old people many times can be avoided if these principles are followed

## HYPERTENSION

Diet faddists draw many followers from this large group and in consequence much nonsense continues to be preached by radio programs and magazine articles regarding the cure of hypertension by dietary measures The main darts are directed toward the proteins (the red meats of the trolley car conversations) and salt although fats and carbohydrates are not neglected

Protein restriction has enjoyed a long popularity It has appeal and in the American home where meat appears in such abundance it may have some value In patients with hypertension who show good renal function, no nitrogen retention and slight if any cardiac damage great restriction of proteins is certainly not indicated However so deeply do press and radio influence the American public that to make a statement of this nature to a patient of the hypertensive type trained in the present belief is usually sufficient to undermine confidence at once The hypertensive tourist of physicians offices will usually co-operate in the matter of drug therapy (so many times not indicated) and may even agree to a major operative procedure yet he cannot be induced to eat meat

Experimental evidence fails to show that excess of protein tends to elevate the arterial pressure On the other hand a low protein diet long continued may lower the blood pressure but this is accomplished through the anemia and physical weakness that are produced Both of these undesirable end products of faulty dieting may contribute to an earlier cardiac breakdown Cardiac cases following a long term in one of the dietary camps often show marked improvement when induced to take protein Even in the presence of a complicating renal lesion particularly of the nephrotic type with considerable albuminuria the addition of protein to the diet is an important factor in clearing the edema Consequently in the absence of cardiac failure proteins should be retained in the diets of patients suffering from essential hypertension in the amounts recommended for the normal person

Salt restriction is another popular practice with deep roots in the small volumes written to advise the laity in matters medical Extensive investigations again fail to show that rigid salt restriction has any effect on the clinical course of hypertension Neither will excessive quantities elevate the blood pressure Those who have tried living on salt poor diets can attest to the fact that they never look forward to meal time and many ill advised

cardiac patients do poorly because of the anorexia and loss of strength that follow salt free diets A normal intake of sodium chloride should be permitted in the absence of congestive failure During congestive failure patients should be warned against excess quantities of salts and salty foods Seasonings of all kinds should likewise be prohibited Recently the salt in the diet has become a most important consideration when organic mercurial diuretics are employed over long periods (page 90)

If obesity accompanies hypertension the diet is written accordingly otherwise a normal diet should be allowed The patient must be cautioned against overeating and too rapid eating particularly when the anginal syndrome accompanies hypertension Fluids need not be restricted in the absence of congestive failure although too much fluid should not be allowed

## OBESITY

Obesity is a well recognized handicap to the patient who has cardiac disease While the extra weight in itself is a burden to the heart the increase in the size of the surface area in these cases places an additional load on the peripheral circulation The extra fat accumulating about the heart may also interfere with its free contraction and infiltrate the organ with further impairment in function

Treatment of the obese cardiac patient by dietary measures lessens the work of the heart by lowering the basal metabolism Since protein foods furnish the greatest stimulus to metabolism care should be taken to reduce the intake of this constituent of the diet to the lowest possible figure usually 1 Gm or less per kilogram of ideal or predicted weight

Reduction of the diet should be brought about gradually The caloric need of the patient should always be calculated and a diet prescribed that is below this basic level It is well to proceed slowly by choosing a diet at first that contains a fairly high allowance Carbohydrates should be given to the extent of 0 6 Gm for every gram of protein to maintain nitrogen balance for carbohydrate in this proportion acts in the capacity of protein sparer Very little fat is allowed in the diet, and the body is encouraged to use the fat in its depots to make up for the deficient caloric intake Green vegetables supply vitamins and their bulk satisfies hunger Between meals especially at the start of the regime occasional glucose candies may be allowed to provide quickly utilizable energy and to combat exhaustion

If the ambulatory cardiac patient who is overweight can be encouraged to co-operate and lose on the average of six pounds in one month much improvement in the subjective symptoms will follow Diets calculated to provide 1000 to 1200 calories are employed in the majority of cases

In patients who require only mild reduction programs, the qualitative restriction shown in Table XVI* may be sufficient For the convenience of

* Tables XVI to XVIII reprinted from Treatment by Diet by Barborka J B Lippincott Company

Table XVI

SIMPLE QUALITATIVE RESTRICTION

TYPICAL FOODS ALLOWED IN REDUCTION DIETS

Milk skimmed and buttermilk
Egg
Meat lean
Meats low in fat as
  Chicken—lean portion
  Liver
  Fish other than salmon
  Shrimp
  Crabmeat
Fruit 5 and 10%
Vegetables 3 and 6%
Clear soup

TYPICAL FOODS TO AVOID IN REDUCTION DIETS

Sugar and All Sweets
Starches as
  Bread
  *Cereals*
  Macaroni
  Spaghetti
  Pastry pie cakes
  Sweet desserts
Vegetables High in Carbohydrates as
  Potato
  Shelled peas
  Shelled beans
  Corn
  *Parsnips*
Fats as
  Butter
  Salad oils
  Cream
Meats high in fat as
  Pork
  Lamb chops with large amounts of fat

the reader a classification of the fresh fruits and vegetables according to their percentage of carbohydrate content has been included (Table XVII) A few sample reduction diets suggesting the amount and distribution of the daily food allowance that may serve as patterns when writing these dietary prescriptions will be found in Tables XVIII XIX XX

## RHEUMATIC HEART DISEASE

The dietary regime in patients suffering from active infection should be planned to combat the wasting effect of the long febrile siege All the food that can be comfortably and safely taken should be allowed and in this regime carbohydrates predominate since every effort is made to keep up body weight Vitamin C has been claimed to have a direct relationship to rheumatic infection and has been given in large amounts in the diets of these patients but I have never seen any marked benefit follow its administration Fluids should be given freely owing to excessive sweating and

TABLE XVII

CLASSIFICATION OF FRESH VEGETABLES AND FRESH FRUITS ACCORDING TO PERCENTAGE OF CARBOHYDRATE CONTENT

VEGETABLES

| 3% | 6% | 15% | 20% |
|---|---|---|---|
| Asparagus | Artichoke French | Parsnips | Corn |
| Beet Greens | Beet | Salsify | Garlic |
| Broccoli | Carrot | Pea | Horseradish Root |
| Brussel Sprouts | Celeriac | | Potato |
| Cabbage | Dandelion Greens | | Dried Bean |
| Chinese Cabbage | Kale | | |
| Cauliflower | Kohl Rabi | | |
| Celery | Leeks | | |
| Cucumber | Onion | | |
| Eggplant | Parsley | | |
| Endive | Pea (tiny) | | |
| Lettuce | Pumpkin | | |
| Marrow | Rutabaga | | |
| Mustard Greens | String Bean (mature) | | |
| Green Pepper | Squash | | |
| Okra | Turnip | | |
| Radish | | | |
| Sauerkraut | | | |
| Sorrel | | | |
| Spinach | | | |
| String Bean (tiny) | | | |
| Summer Squash | | | |
| Tomato | | | |
| Watercress | | | |

FRUITS

| 5% | 10% | 15% | 20% |
|---|---|---|---|
| Muskmelon | Blackberry | Apple | Banana |
| Honeydew | Cranberry | Apricot | Fig (fresh) |
| Watermelon | Gooseberry | Blueberry | Grape Juice |
| Rhubarb | Grapefruit | Cherry | Fresh Prune |
| *Avocado | Lemon | Currant | |
| | Lime | Grape | |
| | Orange | Guava | |
| | Papaya | Huckleberry | |
| | Peach | Nectarine | |
| | Pineapple | Papaw | |
| | Strawberry | Pear | |
| | Tangerine | Plum | |
| | | Quince | |
| | | Raspberry | |

* Avocados contain 17.2 per cent fat

an increase in the sodium chloride intake is good therapy for the same reason.

## CARDIOVASCULAR SYPHILIS

The drastic "cures" for aneurysms recommended by early writers included strenuous dietary measures as well as rest and venesection. Fluid and food were reduced to extremely low levels in the regime originally suggested by Albertini and Valsalva in the seventeenth century (page 252). Today no particular dietary program for cardiovascular syphilis is recom

TABLE XVIII

REDUCTION DIET

FOR EXPECTED OR IDEAL WEIGHT OF 160 POUNDS

**800 Calories**

*Suggested Distribution of the Total Food Allowance for One Day*

| | | Grams |
|---|---|---|
| **BREAKFAST** | | |
| Fruit 10% | 1 serving | 100 |
| Egg | 1 | 50 |
| Egg whites | 2 | 66 |
| Bread | ½ thin slice | 10 |
| Butter | ¼ square | 3 |
| Beverage—coffee or tea | | |
| **LUNCHEON** | | |
| Meat (low in fat) | 1 large serving | 90 |
| Vegetables 3% | 2 small servings | 150 |
| Fruit 5% | 1 serving | 100 |
| Milk (skimmed) | 1 glass | 200 |
| **DINNER** | | |
| Meat (lean) | 1 large serving | 90 |
| Vegetable 6% | 1 small serving | 75 |
| Salad vegetable 3% | 1 small serving | 75 |
| Fruit 10% | 1 serving | 100 |
| Milk (skimmed) | 1 glass | 200 |

TABLE XIX

REDUCTION DIET

FOR EXPECTED OR IDEAL WEIGHT OF 160 POUNDS

**1 000 Calories**

*Suggested Distribution of the Total Food Allowance for One Day*

| | | Grams |
|---|---|---|
| **BREAKFAST** | | |
| Fruit 10% | 1 serving | 100 |
| Bacon | 1 slice crisp | 5 |
| Egg | 1 | 50 |
| Bread | ½ thin slice | 10 |
| Butter | ½ square | 5 |
| Beverage—coffee or tea | | |
| **LUNCHEON** | | |
| Meat | 1 large serving | 90 |
| Vegetables 3% | 2 small servings | 150 |
| Butter | ½ square | 5 |
| Fruit 10% | 1 serving | 100 |
| Milk (skimmed) | 1 glass | 200 |
| **DINNER** | | |
| Meat | 1 large serving | 90 |
| Vegetable 6% | 1 small serving | 75 |
| Salad vegetable 3% | 1 small serving | 75 |
| Butter | ½ square | 5 |
| Fruit 5% | 1 serving | 100 |
| Milk (skimmed) | 1 glass | 200 |

TABLE XX

REDUCTION DIET

FOR EXPECTED OR IDEAL WEIGHT OF 160 POUNDS

1 200 Calories

*Suggested Distribution of the Total Food Allowance for One Day*

| | | Grams |
|---|---|---|
| BREAKFAST | | |
| Fruit 10% | 1 serving | 100 |
| Bacon | 1 slice crisp | 5 |
| Egg | 1 | 50 |
| Bread | ½ thin slice | 10 |
| Butter | 1 square | 10 |
| Cream 20% | 1 tablespoon | 15 |
| Beverage—coffee or tea | | |
| LUNCHEON | | |
| Meat | 1 large serving | 90 |
| Vegetable 3% | 2 small servings | 150 |
| Butter | 1½ squares | 15 |
| Fruit 10% | 1 serving | 100 |
| Milk (skimmed) | 1 glass | 200 |
| DINNER | | |
| Meat | 1 large serving | 90 |
| Vegetable 6% | 1 small serving | 75 |
| Salad vegetable 3% | 1 small serving | 75 |
| Butter | 1½ squares | 15 |
| Fruit 5% | 1 serving | 100 |
| Milk (skimmed) | 1 glass | 200 |

mended The content of the diet prescription is entirely governed by the patient s weight and the presence or absence of congestive cardiac failure We must admit however in the light of modern discoveries of the physiologic chemists, that the old starvation treatment of Albertini and Valsalva was not without its effect on the basal metabolism blood pressure and pulse rate and certainly must have produced in this manner the favorable (although temporary) effect they claimed for it

## DIET IN CONGESTIVE FAILURE

With the onset of congestive failure diet is a most essential part of the management When the patient is first seen the presence of dyspnea and alimentary tract congestion generally places the thought of food in the background

At the start the fluid intake should be restricted It is a custom to begin treatment of congestive failure with the diet originally proposed in 1866 by Karell a Russian court physician While not originally prescribed for patients with this type of heart disease but rather for "les hydropsies de toute natur " Karell s diet consisted of skimmed milk divided into four feedings of 200 cc each given at 8 A M 12 M 4 P M and 8 P M This regime furnishes 26 Gm of protein 1 6 Gm of NaCl 800 cc of fluid and approximately 550 calories It may be continued for one or two days Pa

tients who cannot take milk may substitute other articles to make up a total of the same caloric value from the following list orange juice cereal gruel (Pablum*) thin cream soups or buttered toast As a rule it is well to restrict the fluid intake to 1200 cc during the first 24 hours When satis

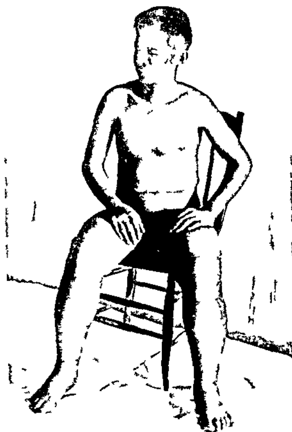


Fig 163 B ibe i (Wet type) (Courtesy Phil pp ne Bureau of Science )

factory diuresis has been obtained the fluid intake may be increased to an extent compatible with comfort and the total urinary output

When improvement in the patient s condition occurs little further attention is usually given to diet However the amount and type of food ingested is most important at this stage and greatly influences the cardiac mechanism through its effect on the basal metabolism Undernutrition in normal

* Mead Johnson Company

individuals has been shown to be accompanied by a fall in the pulse rate, blood pressure and metabolic rate. These alterations follow a slight weight loss and appear even though the usual activities are unrestricted. If we produce similar physiologic alterations during convalescence from congestive failure we shall greatly aid cardiac recovery. Consequently restriction of the diet for the first two or three weeks of the patient's convalescence is helpful. Proger[307] advises first a severe and then a more moderate dietary restriction over this period, so that about 10 per cent of the patient's body weight is lost. In three weeks the patient should be raised to a maintenance diet. During this entire period, fluids may be restricted, for a drop in the level of fluid exchange causes the patient to drink less.

This temporary regime of undernutrition produces in the cardiac patient who is convalescing from an attack of congestive failure a further slowing of the pulse beyond the degree obtained by bed rest and digitalis and an additional increase in blood pressure. The cardiac output is less and the condition of the heart improves because it has less work to do at the lower metabolic level. In addition, as weight is lost, the vital capacity increases. Measurements in some cases may show a decrease in cardiac size. When the same dietary principles are employed in ambulatory cardiac patients, an improvement in the exercise tolerance is noted. During the first days of the dietary restriction, hunger and weakness may be prominent subjective complaints. The co-operative patient is usually satisfied with the diet when its purpose is explained, especially if the improvement is evident following the loss of weight.

If the patient has had several attacks of congestive failure and considerable weight has already been lost, the period of undernutrition should be omitted and the diet kept above maintenance levels. Obese patients many times do not experience the beneficial effects above described. The best results may be obtained in cases where the patient is normal in weight or slightly above the normal, although individual variations in this response may occur.

Table XXI

MODIFIED KARELL DIET

| | | Grams |
|---|---|---|
| **Breakfast** | | |
| Bread (toast) | 1½ thin slice | 10 |
| Fruit 10% | 1 serving | 100 |
| Sugar | 1 teaspoon | 5 |
| Egg | 1 | 50 |
| **Luncheon** | | |
| Bread (toast) | 1½ thin slice | 10 |
| Cream soup | ⅔ cup | 150 |
| Butter | ½ square | 5 |
| **Dinner** | | |
| Bread (toast) | 1½ thin slice | 10 |
| Milk | 1 glass | 200 |
| Butter | 1 square | 10 |
| Egg | 1 | 50 |

The diets shown in Tables XXI XXII XXIII may be used as patterns when variations of the Karell diet or increase in the caloric intake are called for following an attack of congestive failure

TABLE XXII
HEART DISEASE
CARDIAC DIET I
**45 Grams Protein**
**1 400 Calories**
*Suggested Distribution of the Total Food Allowance for One Day*

| | | Grams |
|---|---|---|
| BREAKFAST | | |
| Fruit Juice 10% | ¼ glass | 50 |
| Cereal (cooked) | ½ cup | 105 |
| Egg | 1 | 50 |
| Bread (toast) | 1 thin slice | 20 |
| Butter | ¼ square | 5 |
| Cream 20% | ¼ cup | 60 |
| Beverage—coffee substitute | | |
| 10 00 A M Fruit juice | ½ glass | 100 |
| LUNCHEON | | |
| Soup | | |
| Vegetable puree 3% or 6% | 1 cup | 100 |
| Milk | ½ glass | 100 |
| Butter | ½ square | 5 |
| Egg or egg substitute | 1 | 50 |
| Bread (toast) | 1 thin slice | 20 |
| Butter | ½ square | 5 |
| Fruit puree 10% or 15% | ½ cup | 100 |
| 3 00 P M Milk | 1 glass | 200 |
| DINNER | | |
| Fruit juice 10% | ¼ glass | 50 |
| Milk toast | | |
| Milk | 1 glass | 200 |
| Toast | 1 thin slice | 20 |
| Butter | ½ square | 5 |
| Custard | ½ cup | 100 |
| Bedtime Fruit juice | ½ glass | 100 |

The principles that guide the physician in his selection of a suitable dietary regime for the patient convalescing from an attack of congestive failure may be briefly summarized as follows add to the intake gradually always keeping below basal requirements This may be done by giving frequent small feedings thus avoiding the strain that large meals place on the cardiac reserve The cardiac muscle requires an abundance of carbohydrates (glucose) for its recovery and this constituent of the diet should be proportionately increased While moderate restriction in fluid intake is essential as long as edema can be demonstrated clinically it is most important during this period to keep the salt intake low However if large amounts of mercurial diuretics are being given care should be taken not

TABLE XXIII

HEART DISEASE

CARDIAC DIET II

50 Grams Protein

1 800 Calories

*Suggested Distribution of Total Food Allowance for One Day*

| | | Grams |
|---|---|---|
| **BREAKFAST** | | |
| Fruit 10% | 1 serving | 100 |
| Cereal (cooked) | 2/3 cup | 140 |
| Egg | 1 | 50 |
| *Bread (toast)* | *1 thin slice* | 20 |
| Butter | 1 square | 10 |
| Sugar | 1 tablespoon | 15 |
| Jam | 1 tablespoon | 15 |
| Cream 20% | 1/4 cup | 60 |
| Beverage—coffee substitute | | |
| **LUNCHEON** | | |
| Meat | 1 small serving | 45 |
| Potato or substitute | 1 small serving | 75 |
| Vegetable 3% or 6% | 2 servings | 200 |
| Bread | 1 thin slice | 20 |
| Butter | 1½ squares | 15 |
| Dessert | 1 serving | 100 |
| Milk | 1 glass | 200 |
| 3 00 P M Fruit 10% or 15% | 1 serving | 100 |
| **DINNER** | | |
| Potato or substitute | 1 small serving | 75 |
| Vegetable 3% or 6% | 1 serving | 100 |
| Bread | 1 thin slice | 20 |
| Butter | 1 square | 10 |
| Fruit 10% or 15% | 1 serving | 100 |
| Milk | 1 glass | 200 |

to restrict the intake of sodium chloride too drastically for copious diuresis may give rise to symptoms associated with hypochloremia Protein foods should be given sparingly owing to their specific dynamic action on metabolism Fats should be decreased to a minimum because of difficulty in their assimilation in the presence of the slowing of all the digestive processes

## THE HEART IN DEFICIENCY DISEASES

Feeding experiments carried out on laboratory animals have shown that a variety of symptoms may be produced by diets that are lacking in one or more of the vitamins Similar symptoms have been observed in man when diets deficient in these substances have been taken over long periods

Rarely is the clinical picture so clear cut and definite that the exact deficiency is immediately recognized Usually the patient is found to be suffering from a combination of several deficiencies If we consider the effect of vitamin deficiency on the function of the circulation our attention will be focused mainly on vitamin $B_1$ for in the light of recent studies this is the

chief vitamin deficiency associated with major disturbances of the cardiovascular system

Isolation of vitamin B followed investigations of the cause of beriberi This substance was therefore known as the antiberiberi vitamin Still later discoveries proved that vitamin B was a complex substance made up of two or more factors differentiated on the basis of sensitivity to heat The antiberiberi vitamin was designated $B_1$ and the newly isolated substance as vitamin B or antidermatitis vitamin or pellagra preventing (P P) factor Substances like wheat germ yeast whole meal cereals nuts egg yolk liver heart and kidney are rich in vitamin $B_1$ However it may be said that substances rich in one vitamin of this complex also contain varying amounts of the others

In reviewing the circulatory abnormalities that follow a diet deficient in the $B_1$ factor let us consider first the effect of a marked deficiency This results in the disease picture known as beriberi that is commonly encountered in many of the rice eating countries of the East China Japan India the Philippines and the Dutch Indies and less frequently in other countries Beriberi can occur in mild or severe forms causing partial or complete deficiency states at any age or in any race where poverty and ignorance prevail It is frequently associated with a diet of refined cereals for in the milling process the germ of the grain containing the vitamin is removed

In many ways beriberi is a curious disease Variable factors such as age locality type of work and nationality appear greatly to influence the clinical picture and this is particularly true in respect to the cardiovascular system In the infant beriberi usually runs an acute course There may be sudden diminution of urine rigidity of the body dyspnea and cyanosis Weakness rapid pulse and edema of the legs may develop quickly and in the absence of prompt treatment sudden death may occur In the adult the picture is quite different The onset is insidious with vague and general symptoms of fatigue indigestion mild grades of dyspnea tachycardia and tenderness over the muscles Later symptoms pointing to the involvement of the nervous system may develop and degenerative changes appear in the peripheral nerves When neuritis predominates the condition is known as the dry type of beriberi In contrast to this course another patient may show a predominance of cardiovascular symptoms dyspnea marked cardiac enlargement with dilatation and fluid in the serous cavities This is the so-called wet type (Fig 163) Some observers claim that this form is more apt to develop in young adult males engaged in strenuous occupations where neuritis does not appear early and force the patient to rest Gastro intestinal symptoms such as anorexia diarrhea and vomiting may occur in both types

Wenckebach studying a number of advanced cases in Java with Aalsmeer[389] attempted to correlate the clinical and autopsy findings of beriberi and described the cardiac enlargement and edema He popularized the term beriberi heart Wenckebach likewise called attention to the fact that

the active muscles appear to suffer most in this disease the soleus, the masseter, the gastrocnemius, and finally the heart

Lack of vitamin $B_1$ causes the heart to lose its power of vigorous contraction, its tone decreases and this is soon followed by dilatation If we examine the changes that take place in the cardiac tissue and compare them with those observed in the nervous system we shall find that they are quite similar Sections of cardiac muscle in beriberi show swelling of the cells caused by retention of water a condition that differs from ordinary edema At autopsy, Wenckebach's cases showed dilatation of the right side of the heart the right ventricle, the right auricle and the conus arteriosus were seen literally to be "blown up because of the high pressure on the venous side prior to death

If we view the clinical symptoms in the light of these interesting and curious autopsy findings the state of the circulation in beriberi becomes evident At the onset there is only slight edema all forms of exertion are poorly tolerated but if they are continued edema increases and pulsation will be noted in all peripheral vessels Rest is immediately beneficial in these cases whereas adrenalin exerts a particularly unfavorable influence When this drug is injected even in small doses, the diastolic pressure falls promptly to zero, and a pistol- hot sound appears in the femoral vessels After vitamin $B_1$ is administered in curative doses in advanced beriberi this reaction to adrenalin disappears in most instances

These observations suggest that in the wet type of beriberi all the arterioles are widened The blood literally runs from the arteries into the capillaries and veins Consequently the systolic energy of the heart is not spent in the capillary bed and the blood pours into the right heart behind a considerably increased venous pressure Wenckebach described in these cases a venous hum in the neighborhood of the crural vein produced by the increased velocity of the venous blood The sudden high venous tide causes overloading of a right heart that is already seriously affected by the vitamin $B_1$ deficiency This explains the 'blown up appearance found at autopsy

Studies carried out in this country recently have shown some aspects that correspond exactly to these views A normal or increased velocity of the blood flow with a low arteriovenous oxygen difference have been consistently observed This is in keeping with the impression that there is present in the wet type of beriberi a general arterial dilatation The circulation time is an important point in the differential diagnosis between the wet type of beriberi and congestive heart failure Improvement of the patient following administration of vitamin $B_1$ in beriberi is attended by an increase in the circulation time

Posterior lobe of the pituitary (pitressin) has a striking effect on the circulatory disturbances of beriberi Following the injection of this substance the rapid blood flow is checked on the arterial side and the patient notices immediate subjective improvement The heart rate is slowed the diastolic pressure increases the venous pressure falls the venous hum

disappears and the pistol shot sound is no longer heard In other words the circulation time is slowed and the blood is held longer on the arterial side This of course has raised the question Is the circulatory picture of beriberi due to a decrease of production of the hormone from the posterior lobe of the pituitary gland?

Undoubtedly since the depression years many cases which show cardio vascular symptoms following marked vitamin $B_1$ deficiency have occurred in this country Scott and Hermann[336] observed cases among the rice workers of Louisiana Riesman and Davidson[315] have also reported cases and an instance in a diabetic is recorded by Wohl[419] Nearly every physician will occasionally meet patients who show signs of congestive failure in the absence of a valvular defect or increase of blood pressure or other obvious cause *In all of these instances the nutritional history should be carefully* elicited The patient may be a mixed type and give signs or symptoms of a deficiency state other than cardiovascular for example neuritis or a dermatitis of the pellagra type Various gastro intestinal symptoms may appear If the diagnosis is correct all symptoms should improve following the administration of vitamin $B_1$

As we would expect the electrocardiogram reflects the changes that take place in the circulatory system Lately a variety of alterations have been described in the literature Most cases show a sinus tachycardia with a tendency to T wave alterations Some of the T wave alterations that have been encountered in deficiency states suggest coronary occlusion so it is most important to review the clinical findings in all cases which show electrocardiograms of this type In the deficiency states the waves are apt to change more quickly following treatment than they are usually observed to do in the presence of coronary disease Consequently the dis appearance of electrocardiographic deformities following the administra tion of vitamin $B_1$ is a valuable point in differential diagnosis

Weiss and Wilkins[396] described four patients who experienced attacks of syncope in addition to other cardiac manifestations of the deficiency state These patients were found to have a hyperactive carotid sinus reflex (page 379) the slightest stimulation producing asystole and syncope Administration of vitamin $B_1$ abolished the hyperexcitability at once in three of these patients

Considering the number of vitamin $B_1$ preparations now on the market it is interesting to inquire into the effect of vitamin $B_1$ on the normal heart Experiments to determine this have been carried out and very large doses administered to control patients have been found to have no effect on the pulse rate blood pressure electrocardiogram velocity of the blood flow or serum protein and no untoward symptoms have been produced

In many of the cases published in America which show marked cardio vascular symptoms accompanying deficiency of vitamin $B_1$, alcohol has played a major role Alcohol per se is incapable of causing any effect on the heart of laboratory animal or of man However by reason of the large consumption of alcohol diets deficient in vitamin $B_1$ have been taken

by these patients over long periods Today both the neuritis common in alcoholism and the cardiac changes present at times in the same cases are believed to be caused by the vitamin $B_1$ deficiency However, many have shown a polyneuritis before the circulatory changes entered the picture The diets of many of these patients will be found to average well over 4000 calories consequently they may appear to be well nourished in the presence of a grave deficiency

It is important to remember that patients suffering from any type of cardiac disease may have a superimposed deficiency state and congestive failure may be precipitated by this condition Vitamin $B_1$ deficiency should be suspected, particularly in alcoholic patients when the cardiac findings fail to explain the signs and symptoms A therapeutic test of the administration of the vitamin is in order

## ILLUSTRATIVE CASES

The following histories are typical and illustrate types of $B_1$ deficiency that are occasionally met In the first case the diagnosis was not made or suspected The second patient examined at a later date was recognized and proper treatment resulted in rapid improvement

**Case 108** T M age 68 a retired real estate operator lived on a quart of whiskey a day for two months prior to examination (1934) He complained of cough progressive dyspnea and edema

PHYSICAL EXAMINATION showed a normal blood pressure a pulse of 100 with frequent premature contractions marked edema of face and legs and a questionable ascites The heart was moderately enlarged to percussion in all diameters and a blowing systolic murmur was present over the mitral area Urine complete blood count and blood Wassermann reaction were negative

COURSE The patient was placed at bed rest and given digitalis and diuretics which had no effect on his circulatory symptoms His supply of whiskey was difficult to control Removal to a seashore rest home elimination of the whiskey and a normal diet quickly restored his balance The type of circulatory failure was unexplained at this time Follow up examination of the patient (1937) revealed a normal cardiovascular system His wife volunteered the statement that his symptoms recurred in their entirety the previous year when he started drinking again and not eating for three months A normal diet again efficiently removed all signs of congestive failure

**Case 109** J C age 39 a salesman was treated for some years for peptic ulcer with the usual dietary restrictions Gradual loss of weight resulted He was first seen following a vacation during which he consumed considerable quantities of alcohol He took very little solid food during the course of a month He was unable to return to work at the end of this time because of palpitation tachycardia swelling of the hands face and feet and marked dyspnea Previously his exercise tolerance had always been excellent and the history was negative for cardiac disease

PHYSICAL EXAMINATION The blood pressure was found to be low the heart slightly enlarged, and a systolic murmur was present over the aortic area Blood count blood Wassermann reaction and urine were negative

COURSE Hypodermic injections of 30 milligrams daily of thiamin chloride with a diet rich in vitamin B brought marked improvement The patient returned to work in two weeks Subsequent roentgen ray examination revealed a duodenal ulcer necessitating a further adjustment of his dietary regime

## RICKETS AND SCURVY

Rickets may cause cardiac dilatation and failure In children who die suddenly from this disease ventricular dilatation is commonly found at autopsy As a rule rickets is not dangerous to life but deformities may be lasting and when they occur in the chest they may be the cause of alterations in the position and function of the heart

In scurvy cardiovascular symptoms may arise secondary to the anemia not uncommon in this disease or hemorrhage into the pericardial sac Death in some cases may be caused by cardiac failure However Weiss and Wilkins analyzing a control group of 110 cases of scurvy uncomplicated by other types of vitamin deficiency failed to find a single case exhibiting the circulatory abnormalities described here as suggestive of deficiency disease[386]

# 22

# THE SENILE HEART

Sleep after toil port after stormy seas,
Ease after war death after life does greatly please
—SPENSER, *The Faerie Queene* Bk 1 Canto ix, st. 40

Geriatrics deals with the problems of senescence and senility, and usually fails to attract physicians who are searching for special fields of research While questions relating to infancy and childhood are completely studied by well equipped hospital groups and described in separate journals those connected with the sunset of life receive much less attention However there are many therapeutic items of importance in geriatric practice that deserve special consideration Most of them are covered in the limited number of good treatises on the subject of geriatrics, and all are admirably summarized in a recent contribution by Pepper [794] Only problems relating to the cardiovascular system will be briefly considered here

## TYPES

The heart does not share the tendency to atrophy that is present in many other organs of the body as age advances its relation to body weight remains the same Older writers held the opposite view and believed that the heart and arteries underwent hypertrophy Even among physician of today there is a prevailing opinion that continued increase in the blood pressure takes place with advancing years On the contrary, it has been found that the pressures show only slight elevation until the sixth decade and then remain unchanged in the absence of disease the average pressure readings staying at 130 to 140 systolic and 80 to 90 diastolic There is a slight decrease in the pulse rate in the later decades

The change that may be clearly visualized in the senile aorta at the time of fluoroscopy is generally caused by a deposition of calcium in the media Similar alterations occur in the peripheral arteries and are associated with little interference in the passage of blood This condition of the media is known as Monckeberg s sclerosis and should not be confused with atheroma

ATHEROSCLEROSIS OR ATHEROMA involves the intima and may be present in younger individuals Intimal deposits of lipoid material first appear and subsequently undergo softening with a discharge of their contents into the lumen of the vessel An atheromatous ulcer then forms and this lesion paves the way for thrombus formation and embolism The aorta is the most frequent site of atheromatous lesions (see Fig 111)

but their occurrence in the coronary arteries is of considerable more importance to the clinician (see Fig 107) Other types of heart disease (rheumatic syphilitic or congenital) are practically unknown after 70 years of age

While heart disease in old age is very closely allied to arterial degenerative changes by no means all old people show advanced atheroma On the other hand atheromatous changes of extensive degree are sometimes found in young individuals Further discussion of the causes of this early degeneration of the vital arterial structures would lead us into deep water Perhaps it is in some measure due to the speed of living of the person whose arterial inheritance is poor It may appear earlier when tobacco and alcohol are used in excessive amounts Degenerative changes on the other hand may be greatly delayed in those who use these substances in moderation eat sparingly and avoid the hurry and worry of modern existence The speed of living is not so much in evidence among inhabitants of tropical and subtropical countries and this may in part explain the lower incidence of hypertension and arterial disease in these regions

## EXAMINATION

The examination of the heart in older patients is not easy In the first place there is usually a rigid thorax with more than a little accompanying emphysema which makes it difficult or impossible to locate the apex beat For the same reason if percussion is attempted the markings of the cardiac borders that are obtained are usually found to be unreliable An orthodiagram or roentgenogram is quite often needed to determine accurately the cardiac size In the aged, the heart sounds are many times recorded as distant and weak when frequently this change is only a result of the emphysema and in some instances the thickness of underlying tissues of the chest wall Systolic murmurs that have little significance are often present

If we study the anastomotic connections of the coronary tree we note that they increase in number with advancing years This accounts for the smooth course often observed when occlusions develop in old people Frequently coronary changes progress to a marked degree without producing symptoms in aged individuals Even thrombosis appearing as a complication during the course of this disease may be almost harmless Mild degrees of angina in the aged are as a rule easily controlled mechanisms and many of the cases are never seen by the physician for the reason that is usually stated At my age I shouldn t run to the doctor with every ache and pain I expect to have a few

**Other subjective symptoms** that may accompany the aging process are paroxysmal dyspnea acute pulmonary edema and congestive failure Extrasystoles are present in many cases in some instances they may be as common as the remaining gray hairs They are seldom noticed by the

patient and are usually unimportant Often they can be controlled if proper attention is given to the diet and elimination

**Heart Failure** Hypertension produces a left ventricular enlargement and the signs of failure are apt to develop swiftly in some cases following very severe unaccustomed exertion The right sided failure of pulmonary heart disease may add cyanosis and venous engorgement to the picture

**A sclerosis of the heart valves** takes place in old people and at times it may advance to a considerable degree in the aortic valve with calcium deposition particularly if the valve has been previously damaged by rheumatic invasion The structure protrudes into the blood current in these instances, and produces a systolic murmur in the aortic area A more advanced lesion may be accompanied by the typical signs of aortic stenosis (page 127)

**Aneurysms** While aneurysms are as a whole uncommon in old age, the dissecting type may occasionally occur and cause sudden death The dissecting aneurysm begins with a split in the intima the blood column usually forcing its way through a necrotic area in the media less often near the margin of an atheromatous patch In this manner the aorta may be dissected in either direction by the column of blood While rupture and death are the usual sequelae in very rare cases organization may take place (page 322)

### Electrocardiogram

Changes in the electrocardiogram may accompany the aging process The voltage becomes reduced the T waves lowered and the QRS complexes as well as the P R intervals show slightly increased duration Changes of this degree are not unusual in senescence Levitt studied 100 men and women in the late decades of life whose histories and physical examinations revealed no evidence of heart disease and discovered that 26 per cent showed definite electrocardiographic abnormalities Willius[408 409 414] reviewed the electrocardiograms of 700 patients over the age of 74 and found that 55 per cent had abnormal tracings

## TREATMENT

The management of the aged patient who has cardiac disease requires *tact diplomacy and skill It is most important first* of all that these patients should be encouraged to keep active and should not be permitted to remain in bed for long periods unless congestive failure or an acute coronary occlusion occurs The physician fails to realize that old people like attention and no matter how gloomy their prognosis they should not be neglected in the daily rounds It should be a constant rule of practice not to disturb their habits of living We should not go to see them in haste with the attitude of a dictator and should not prohibit the old man (or woman) from smoking unless the circumstances in the case indicate the need for the step The same applies to the diet It should be

regulated with tact but much latitude should be allowed unless diabetes is present In this event too severe a restriction of carbohydrate at the start will be likely to be followed by untoward symptoms Fluid should not be restricted unless congestive failure is present If obesity exists we should not hound the patient to start a diet that may send him to his grave but should be tolerant and congratulate him on the good cardio vascular apparatus that he possesses in spite of the handicap of age and weight With this attitude the essential changes in the daily program may be more readily instituted

**Daily Regime** Regulation of the daily regime is all the treatment that is required when mild degrees of structural change in the cardio vascular apparatus are discovered on routine examination Mild dyspnea that is indicative of a decreased myocardial reserve may usually be con trolled by adjusting the exercise allowance (Chapter 20) While the functional capacity of the heart is often reduced in the aged this may not be evident because of the restrictions placed on activity either by advanc ing age or ome accompanying degenerative process like arthritis Al though a reasonable amount of exercise is quite beneficial and is responsi ble many times for the ability of old people to carry on unaccustomed or prolonged activity is unwise The ranks of the Blue and the Gray always thin rapidly after the forced marches of Memorial Day or the unaccus tomed activities of anniversary encampments

**Drugs** Great care should be exercised in the drugs that are given to aged patients and too great therapeutic activity should be avoided at all times

DIGITALIS This is particularly true of digitalis for toxic symptoms are apt to develop very early in the aged While nausea and vomiting may occur following small doses cerebral symptoms are very apt to appear (page 79) Even in the presence of congestive failure digitalis should be given slowly and carefully for older patients require much smaller doses Digitalis should never be given to old people in the absence of congestive failure or fibrillation

Before using mercurial diuretics kidney function should be determined In old men an active diuresis may cause retention so the output should be carefully watched following the administration of any of the organic mercurials If prompt response to the diuretic is not obtained always examine the patient for retention of urine and use an in dwelling catheter when necessary

GLUCOSE is of great value in the treatment of circulatory complications in the aged particularly postoperatively and in the presence of congestive failure It is also useful in combating attacks of paroxysmal cardiac dyspnea or cardiac asthma Given intravenously in amounts up to 400 cc of a 5 to 10 per cent solution it furnishes food for the heart and helps to replace its glycogen store

MORPHINE is a valuable drug in the treatment of the diseases that are commonly met in the declining years of life We could not do without it

in the presence of inoperable cancer where the pain is great and life expectancy short In heart disease morphine is justified in attacks of dyspnea of the paroxysmal type, but it should be used cautiously Prescriptions for the common and less serious ailments of the aged should never contain morphine, particularly those that are written for bronchitis The drug should always be used with care in pneumonias because of its tendency to produce or increase abdominal distention and to decrease pulmonary ventilation In coronary occlusion morphine should be used in the presence of pain Fenn[90] emphasizes the fact that morphine is more apt to sensitize the vagus and cause reflex coronary constriction and recommends papaverine and atropine In some cases this combination may be entirely effective In other instances it has to be supplemented by the use of small doses of morphine Oxygen administration is of great value in the treatment of coronary occlusion (page 98)

SEDATIVES are many times indicated in geriatric practice, but the dose and the preparation should be chosen with care The acquaintance of the physician with the patient and his habits of living should assist in answering the question as to the advisability of giving whiskey or brandy I have found it valuable in treating cardiac patients of advanced years particularly when the anginal syndrome is present Many times it proves to be efficient when given at bedtime in place of the more commonly used preparations containing barbital

Sedatives of the barbital group have been known to produce mild delirium in many instances, and care should be taken in the amounts that are prescribed for older patients Sodium bromide may be substituted, but is less certain in its action There is no objection to chloral hydrate or paraldehyde and either of these may be used to replace the barbital compounds

**Blood Pressure** Attempts to lower the blood pressure by medication of any type may result disastrously and should not be attempted in the aged since the adjustments to sudden variations in the blood pressure are not as fine in the presence of sclerotic changes (see Case 46) Vertigo and syncope may result or arterial thrombosis in cerebral visceral or peripheral vessels may follow therapeutic efforts of the type that are attended by some slowing of the blood current The increased viscosity of the blood in elderly individuals allows it to adhere readily to the vessel wall and this ever present factor favoring thrombosis should not be given a helping hand by the physician

**Angina** may be completely controlled by regulation of the daily regime If attacks are still experienced small doses of nitroglycerine may be given (page 247) Theophylline ethylene diamine may also be tried (page 270)

**Heart Block** When heart block is accompanied by Adams Stokes seizures, satisfactory management is difficult and the prognosis is usually poor (page 401) Fibrillation in old people is apt to be accompanied by a slow ventricular rate, owing to the decreased power of conduction in the bundle of His The presence of this natural block should make us hesitate to use digitalis if congestive manifestations are absent Quinidine should

never be used to restore normal sinus rhythm in the presence of chronic auricular fibrillation in old people On the other hand quinidine may be life saving in the presence of paroxysmal auricular or ventricular tachycardia

**Delayed Shock** Following even slight accidents old people may develop a syndrome that has been frequently referred to as delayed shock[3, 6] It begins a few days after the accident with symptoms suggestive of a gradual circulatory failure and may terminate in bronchopneumonia Consequently the prognosis of accidents even of trivial character should always be withheld for a few days until this danger period has passed This delayed reaction is not difficult to explain The bed rest restricts breathing and this effect is usually augmented by one or more injections of morphine given for pain following the trauma Stasis develops in the lower lobes of the lungs, and this places extra work on the heart Cardiac failure may be precipitated by infection reaching these lung areas as it often does without much delay unless unusual care is taken

**Surgery** There is an unfortunate tendency on the part of the profession to overrate the danger of surgery in old age When the advisability of operation arises the nature of the contemplated procedure and the cardiovascular status of the patient are usually the first considerations In the common emergencies of old people (acute obstruction acute prostatic retention strangulated hernia) life saving surgery must be recommended However when other operative procedures are contemplated the deciding factor is not the actual age of the patient but the physiologic and pathologic condition of the body as a whole and the circulation and mental state in particular Elderly people should not be denied relief of chronic inconveniences just because of their age for this does not mean that they are poor risks Montgomery and Walters have recently emphasized this point in reporting a series of seven major operations in persons over 70 years of age The patients in this group stood the major procedures very well and all were benefited

If the altered physiologic processes of the aged patient are respected a satisfactory course may be predicted following major surgery It is important to carry out the operative procedures with speed and gentleness and at the same time preserve body temperature and guard against hemorrhage Old people cannot stand blood loss or shock as well as younger patients While shock may appear more slowly reaction to the usual measures for its relief is also a slow and uncertain process However old people usually make good patients for surgery When confronted with an emergency operation they display a much more placid outlook very seldom fear death and show little emotion Moving the aged patient from the hospital to the customary surroundings of the home at the earliest possible time will often be a great aid in the prevention of postoperative circulatory complications

All therapeutic measures whether surgical or medical should always be planned with the age of the patient in mind A multiplicity of remedies for

example even though correctly applied during the course of chronic heart failure may result disastrously where more conservative therapy slowly and cautiously given may be quite efficacious In this respect, when planning the management of a patient of advanced years we should always recall the words of Oliver Wendell Holmes

> 'so—don t in mercy try
> To pump your patient absolutely dry'

# 23

# SOCIAL SERVICE IN THE TREATMENT OF HEART DISEASE

*By* HELEN E HEIKES*

*and*

OLGA TATTERSFIELD§

*The problems involved in the treatment of persons suffering from cardio* vascular disease are common to both urban and rural communities The first problem is the person who is unable to pay the physician s fees and laboratory costs at private rates and it is this type of patient who applies for medical treatment in the heart clinics of the various hospitals of the larger cities Most of these clinics are equipped to render the needed service at a charge within the means of the patient or entirely without cost to him if necessary The clinic physician and his assistants examine the patient make the diagnosis and prescribe the treatment However successful medical treatment depends in some cases on the social factors involved Consequently trained social workers are a necessary addition to the staff in all large hospitals It is their function to help the patient utilize the prescribed medical treatment to the greatest advantage

In a busy heart clinic it is impossible for the physician to be familiar with the personality and social status of each patient The physician outlines the regime of treatment but often obstacles prevent proper execution of these plans Success in treatment may depend on bed rest at home convalescent care a quiet environment and freedom from anxiety better nourishment warmth employment which will not tax the heart and a host of other adjustments The medical social workers concentrate most of their attention on these matters

The first task of the worker is to individualize the patient for the physician Then she supplements the physician s instructions by a detailed interpretation of every item of his diagnosis and treatment It is vitally important for the patient to understand fully his physical condition so that his problems may not be complicated by unnecessary fear of chronic invalidism or sudden death The social worker can also assist the patient in adjusting personality problems frequently the patient has to be helped to express his fears resentments and bewilderments before treatment can be carried on successfully The patient can also be aided in utilizing his community resources with regard to school his occupational and recre

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ational life and the development of all of his capacities as much as possible within his limitations

In looking further into the many aspects of the social worker's role in combating heart disease let us see what can be done about the child who has rheumatic heart disease Although the medical needs are met by clinic or family physician what other factors are involved in his care? Damp, over crowded homes poor physical hygiene, and lack of proper nourishment are certainly not conducive to combating rheumatic infection The child's school life is especially important Children with heart disease should have the maximum opportunity for education with due attention to vocational adaptation in order that they may receive training for gainful occupations that will not prove too great a strain upon the heart muscle Where school adjustments are necessary, the co-operation of the medical organization of the public school system as well as of the principal and teachers must be secured These persons should be acquainted with the physical condition of the child and with the necessary adjustments that will enable him to carry out his school work successfully Sometimes it is advisable to request the use of the school elevator or to transfer the child to a classroom on the lower floor Perhaps the child can easily climb the necessary stairs if allowed to take his time going up and down either before or after the other children Sometimes permission must be obtained to use recess periods for rest periods instead of for the purpose of recreation

At home the child may be the victim of either over anxiety or indifference on the part of the parents Other factors that hinder progress are lack of parental control family friction and the child's resentment of and refusal to accept exercise restrictions also the use by the child of his physical disability as an attention getter in his home and social group Often the social worker must establish a direct relationship with the child in order to assist him in working out his problems Where the home environment is such that the child cannot have adequate care placement in a convalescent hospital or foster home may be necessary

> The physician or clinic is but a hub in the wheel of cardiac treatment and a great part of the problem of the cardiac child is the problem of the home and social and school life'[31]

With the adult we have the problem not of prevention but of adjustments necessary to keep the patient in such condition that he may lead a useful contented life within his limitations Here again the fear element must be overcome not only by the family but by the patient himself Fear of lack of ability to provide for himself and for his dependents fear of chronic invalidism or of sudden death often retard progress The readjustment of the economic status of the patient is also an important social factor in recovery Very often the mother of a family needs help in her daily work convalescent care must be provided and in cases where the patient cannot return to his regular work sheltered employment and occu

pational therapy can be used to aid the process of rehabilitation In some instances the patient can return to his former occupation provided some minor adjustments are made

In the life of the cardiac patient recreational opportunities are important for both adults and children It is vital in making the adjustment to the disease that the patient meet his associates on the basis of what he can do instead of on the level of what he is not permitted to do along recreational lines Too often the cardiac patient tends to become withdrawn because he is too conscious of his physical limitations and it requires skillful teamwork by the physician and the social worker to help the patient to sub ti tute a more limited but satisfying type of recreation for the more active forms he once enjoyed

The following case histories illustrate some of the situations in which the social worker functions in helping the patient to solve the problems that hinder medical treatment *

## ILLUSTRATIVE CASES

**Case 110** Henry K age e ght was referred to a heart clin c by the school doctor A phys cal examination revealed a funct onal heart murmur and the patient was placed n Class F After the examination his moth r asked the do tor the result. He told her b iefly that there v as no cause for v orry but that he would l ke to re-examine Henry in six to e ght month Four months lat r Henry contracted pneumonia and was admitted to the hosp tal When the social worker interv ewed th mother relative to the data the doctor needed to complete the pi ture of his patient she learned that Henry was s llen and d sobedient and had been absent w thout leave from school several times The mother said that she had restri ted his exercise because he had heart trouble forbade him to run roller skate swim play ball etc The doctor had told her not to wo ry but she had heard of people who dropped d ad suddenly of heart disease and the doctor v ould not want to exam ne Henry again if his heart was all right The school do tor also had sa d that Henry had heart t ouble

The social worker was able to expla n to this bew lder d mother that Henry had no o gan c heart lesion that there was no reason to restrict the boy s exercise She also made clear why the doctor had r quested the re-exam nat on The mothe accepted the explana t on and allowed H nry to assume h usual ct vities after he had recove ed from his ill ness When he returned to cardiac clin the orker w nt with him and his mother to the docto and at the examination Henry was discharged from the clin c The mother had an opportunity to talk with the doctor and later v ith the social wo ke and said th t she understood and was entirely satisfi d Needless to say Henry s behav or problems d d not return and he was leading a normal l fe when last seen

**Discussion** This illustrates the average person s conception of heart di ease and the damage which can be done to the individual unless he has adequate interpretation and help from the physician and the social worker

**Case 111** Ed th Y age 11 Diagnos s chorea Class F

Ed th w s bro ght to the hosp tal acutely ill ith chorea nd was adm tted The mother distu bed the hospital administration by v alking up and down in f ont of the

* We h to thank the S cial Servi e D p t ents of the Graduate P nn ylvan a St Ch t ph r nd Woman s College Ho pital of Philadelph a and the Placement Serv ce of the Philadelph a Health Council a d th T berculosis Comm ttee for the case r cord used in this chapte

hospital several hours each day although she could visit only once weekly On being questioned, the mother stated that she could not help herself The doctor explained to the parents the child's diagnosis and told them that she needed prolonged rest that there was no heart damage then and that complete recovery was likely The case was referred to the Social Service Department by the physician, and an appointment was made to see the mother Both parents were very emotional The mother had hyper thyroidism and the husband was a stubborn German type The father blamed the mother for the child's illness and the mother blamed the lack of proper food The worker had to make the parents understand that the hospital did not consider that Edith was ill because of her care at home that the cause of chorea is unknown, but that it can be controlled by proper treatment The parents wished to take the child home against advice several times but after an interview with the social worker they revised their decision

In view of the friction in the home the doctor recommended a long period of convalescent care for the child After much work on the part of the social service department and the physician the child was allowed to go the parents at first refusing because they did not wish Edith to be away from home any longer One month later Mr V informed the social worker that she was taking Edith from the Children's Heart Hospital since her husband was out of work and could not pay the board rate The social worker interviewed the hospital and arranged that the charge for board be cancelled so that Edith could remain as long as necessary Upon Edith's return to heart clinic after discharge from the convalescent home, her condition was good and the parents followed the doctor's recommendations for her home care as interpreted by the social worker

Discussion In this case the value of the social worker is seen

(1) In acquainting the parents with the nature of the child's illness and so preventing withdrawal of the patient from the hospital before convalescence was complete

(2) In arranging for continued convalescent care at the Heart Hospital

(3) In interpreting to the mother the doctor's recommendations for the final home care which are at present being carried out

**Case 112** Roger M age 11 years had been a patient in heart clinic for several years suffering from rheumatic heart disease His exercise was quite restricted and he had little opportunity for school because of long periods in the hospital and equally long periods of bed rest in convalescent hospitals This enforced inactivity bred resentment and he became a thorn in the side of the authorities at several convalescent homes When a third hospitalization became necessary Roger broke out into violent rebellion and temper tantrums

The medical social worker and the physician reviewed the situation and what it meant to Roger The boy's home life was troubled and insecure The father a weak and inadequate person drank to excess and sought to maintain his status as head of the house by bullying his family The mother a wornout household drudge tried to work with the hospital but her efforts were confined to nagging Roger about over stepping his exercise prescriptions Two older sisters added their voices to the family chorus of disapproval of Roger's conduct, which merely served to increase the boy's resentment against the family the hospital and the world where all forces seemed to be gathered against him

It was evident that Roger could not reach an adjustment in such an environment Likewise a return to a convalescent home held no solution to his problem since he was fighting institutionalization and restriction and was having little opportunity for education Foster home placement seemed worth trying and the situation was discussed with an excellent local agency They finally agreed to make placement upon a medical basis Roger continuing his medical care in heart clinic as before

This plan was discussed with Roger and his parents as a medical plan recommended by

the physician and they agreed to it Roger was accordingly placed in a foster family grad ally resumed activity went to school and was seen regularly in heart clinic Throughout this period away from home he was visited by his family and his relationship with them was kept always before him It required several years and three changes of home before Roger was able to work through his problems and make a real adjustment to his disease but he finally was considered well enough and sufficiently balanced emotionally to return home where he has been for several years He managed to remain his standing in school and now enjoys life with a much increased exercise tolerance In addition he has a recognized place in the family and community

Discussion This case shows how serious behavior problems may result at times from over institutionalization and from lack of understanding in the home Individualizing the boy in a foster home with understanding foster parents focused his attention upon his possibilities instead of his handicap so that he realized himself as a part of society instead of one cut off from his fellows by an arbitrary restriction

**Case 113** Edward A colored age 11 years was referred to the heart clinic from medical clinic where a diagnosis of rheumatic heart disease was made The boy was underweight and malnourished and had developed behavior problems at school The home background was lacking in what we consider good child care Edward was an illegitimate child his mother was employed by day and was often absent from home at night Edward was irregular in his school attendance was disobedient disturbed the classroom by antics designed to get attention pilfered small amounts of money from his mother and ran the street until late at night The physician in heart clinic referred the problem to the social worker and the boy to neuropsychiatric clinic

Edward was found to have an IQ of 114 and although a year younger than the other children in his class at school was able to do the required work He had lived with his maternal grandmother until her death and had been with his mother only ten months and was practically the only colored child in the neighborhood His mother gained a degree of understanding of the factors unbalancing the boy's life and decided to give up her work and stay at home a paramour having come into the picture who was willing to support mother and child and for whom Edward had developed a real affection as a father substitute Edward was transferred to another school and did well for a time because teachers and principal interested themselves in his adjustment When they relaxed their attentions Edward's behavior problems gradually reappeared His mother came to the social worker for help because Edward was fighting with the other children missing school stealing and he thought his health must be poor and that there was something wrong with his mind The situation was discussed with the physician on the basis of the child's heart condition while the need of better home supervision and a plan for a foster home placement was worked out with the mother The services of the placement agency were enlisted and Edward was established in a foster home where the foster parents had a good understanding of boys their needs and problems Since placement Edward has gained considerable weight his heart has definitely improved and behavior problems are no longer in the picture He gets along well with other children and the school authorities have no complaints He maintains contact with his mother who visits him frequently

Discussion This picture shows a bright alert colored boy suddenly thrust into an unstable home atmosphere after the death of his grandmother who had reared him Lack of parental supervision unwholesome family relationships and isolation in a community where white people predominated gave rise to the personality difficulties which manifested themselves in antisocial behavior Efforts to help Edward to become adapted to

this environment failing foster home care was carried out and the boy responded to love and a stable home environment, although maintaining contact with his mother

**Case 114** Julia G age 1 Diagnosis rheumatic heart disease with mitral stenosis The findings of the cardiologist and the recommendations for convalescent care were discussed by the social workers with the parents and a plan was formulated wher by Julia was admitted to the Children s Heart Hospital She remained there for four months returning home at the end of that time

Julia lived with her family of seven persons in a congested section of the city in a small house which was in fairly good condition Her parents were Irish American took an intelligent interest in Julia s care and tried in every way to work with the doctor and social worker After Julia s discharge from the Heart Hospital she came regularly to clinic and the parents tried to limit her activity but she was restless and showed a continuous temperature and weight loss that finally neces itated a second hospital ad mission Convalescent care was again advised the parents agreed and Julia was re admitted to the Heart Hospital where she stayed for eight months She returned to school and was placed in a nutrition class at the re uest of the doctor in heart clinic but again she lost weight and did not do well in classes Her father was so fearful of school by this time that conference with the physician of the Board of Education was arranged for him by the social worker and the child was allowed to remain at home for the rest *of the school year (three months) In July she was sent to the Children s Seashore House* f r three weeks

Julia started school again in September did well and reported regularly to heart clinic during the next year and had few set backs She soon began going to dances and lived a normal social life Her cardiac status improved during the next few years At the age of 19 she married Her first baby was stillborn When her second baby was expected she came to the social worker with the request for assistance in obtaining prenatal care and hospital delivery Satisfactory arrangements were made for her hos pital delivery Following this she had two other children has no symptoms referable to the cardiovascular system and now is leading a happy normal life

**Discussion** This case is illustrative of the value of intelligent participa tion by parents and child in a regime of medical care that is formulated by the physician and carried out with the help of the social worker Long term convalescent care and supervision helped to arrest rheumatic activity in this case and the patient led a normal happy life within limitations that were understood and accepted

**Case 115** Eleanor M age nine was admitted to the heart clinic because of mal nourishment and active rheumatic heart disease Investigation of the home environment showed that her mother and father were constantly bickering and had no conception of the child s needs placing upon her all the responsibility for rest and care Since manifestly the child could not progress under such cond tions convalescent care at the Children s Heart Hospital was arranged In a few months the parents demanded the child s return as they were on relief and sought this means of *having their grant in* creased The parents demands were discussed with the chief of the cardiac clinic and he was willing to have Eleanor return home provided she would be kept in bed Eleanor accordingly returned home and a visiting nurse was called in to give her bedside care Milk and additional food for the child were provid d by a private family agency The nurse soon reported that she found that the continuous quarreling of the paren s was affecting the child and retarding her recovery The social worker arranged an interview for the father with the chief of the cardiac clinic who explained to the father the importance of quiet and restfulness for the child at home wh le the social worker brought out similar points in a talk with the mother The parents agreed to give

Eleanor a room to herself a ay from family disturbances and an occupational therapist was also sent in to help her during her enforced rest The child is improving stead ly at this time and her exercise tolerance has increased

**Discussion** This case history again illustrates how family friction can retard a child s recovery and how the social worker can help both parents and the child to a better adjustment

**Case 116** John H a boy of 16 was referred to the Social Service Department of the hospital where he was attending heart clinic by the clinic physician to see hat could be arranged to enable h m to go on with his art work at which he showed great aptitude The boy s family consisted of an indolent father who would not work a mother ho did day s work when she could get it and a sister of 17 who worked regularly and practically supported the entire family The father wanted John to leave school and get a job to help in the suppo t of the fam ly The doctor felt that John needed sedentary work a he had very definite heart damage and could not stand any form of manual labor The so ial worker d scussed this with the family and after many visits persuaded the father to let John go on with his studies provided a scholarship could be secured for him She then took this p oblem to the local heart association and together they secured a scholarsh p for John in art school An interested person offered to pay for the s pplies he needed and his s ster consented to pay h s carefare and inci dental expenses

John spent three years at art school and did very well he received prizes for his prints and honorable mention for his charcoal work After he finished his training a pos tion as secured for him with a firm of engravers but this work proved too arduou and his health began to suffer He was forced to give it up However he proved to be an energetic boy and soon secured some art ork on his own time He is at present free lancing and making a good living for himself and his parents The s ster has married and left the home and John is supporting himself and his parents adequately

**Case 117** Will am G age 19 hen referred to cardiac clinic by the eye clinic was found to be suffering from advanced rheumatic heart d sease The social orker inter viewed Will am and at h req est referred h m to the Bureau of Rehab litation as his heart condition prevented laboriou work The bureau gave no encouragement to the p tient about tra ning for ork with n h s act vity lim tation He was dependent upon h s sister who was resentful of having to prov de fo him and their mother and made life ery unpleasant for both Through the efforts of the so ial worker in heart clin a train ng course at a school of occupational therapy as secured for William and a job provided at the end of the training course by the Shut In Society At this time h developed pneumonia and was adm tted to the hospital He was greatly worried about h s job until the social worker told him that she had found that it would be open for him when he recovered He returned home and to work Later he was upset and de spondent when h s mother became ill After her recovery the patient was in such a poor condition through anxiety that the clin c physic an recommended convalescent care and William agreed to go to a convalescent home In the meantime the s ster who was the d sturb ng element in the fam ly moved away and William and his mother now live a much happier peaceful life although he is at the present time still unable to go back to work and he and h s mother are li ing on a relief grant The clinic physic an feels however that if William continues to improve under the better home condition in time he will be able to resume work and be self supporting

**Case 118** Henry G 29 years old a patient n heart clin c was referred to the Social Serv ce Department by the chief of cl nic to see f some plan could be worked out hereby Henry could earn a living for himself and his family wh ch cons sted of h s wife and three small ch ld en H s physician stated that the ork he was doing in a leather factory was much too strenuous The social worker referred Henry to an employment bureau for the hand capped and the placement worker there finally secu ed a job for

the patient in another factory making small suitcases and bags It was a finishing job, and Henry could sit down while working He has been with this firm for about seven years and is doing well physically as well as economically

**Case 119** William N an unemployed laborer of 66 suff ring from hyp rtensive cardiovascular disease was referred to the Social Service Department by a clinic physician to see if some work could not be secured for him to do at home The patient s heart was not able to stand the strain of employment outside the home but the physician felt that he needed something to keep him occupied The patient lived with a married daughter and her family who had quite a struggle to get along financially The social worker made arrangements for an occupational therapist to visit William and teach him to do some handicraft He was interest d in learning to make hooked rugs and soon became very proficient working on a frame placed in front of his chair at an angle so that there was no strain on his arms William worked at rug making for about three years filling orders that the occupational therapist helped to secure for him and earned between $15 and $30 a month This money was a great help to his daughter as he was able to pay hi board and he was happy and contented in his work William died three years later but we believe that this work probably prolonged his life, since he had been restless and unhappy before he undertook it

**Case 120** Mrs T This patient a widow of 4 was a foreigner who spoke very good English She was referred to heart clinic from the general medical clinic It was found that she had an advanced cardiac lesion and could not continue the domestic ervice in which she had been engaged She had no relatives in this country and no one to help her financially Upon th physician s re ommendation she was admitted to the hospital for a period of several weeks and then sent to a convalescent home in the country for a month s stay The social worker meanwhile got in touch with a family agency and succeed d in g tting a t mporary w kly grant Th worker then referred the patient to an employment agency for the handicapped A vocational guidance test at the local university proved that she was capable of business training A scholarsh p to a business college was then provided and a room was secured for her rear the busine s school The patient quickly and successfully completed the course of study and a job was secured for her by an employment agency The family agency withdrew its grant as the patient became self supporting At the la t report the patient had be ome a valued member of an office staff was happy and satisfied in her work and had entered into the social activities of her community

**Discussion** Had the services of the social worker not been available, this patient could not have made use of the valuable community resources as she knew nothing of such services Her medical treatment, therefore could not have been satisfactory either to doctor or to patient

The foregoing case histories are illustrative of the many social factors which complicate life for the cardiac patient and handicap medical treatment They show also how the physician and the social worker function in the interest of the patient The physician in the conduct of a busy clinic must necessarily relegate the social treatment of the patient to the medical social worker From this point there must be close co-operation between worker and physician in the patient s interest The physician s responsibility is to outline treatment, the social worker duty is to individualize the patient to the physician to consult with the phy ician and to keep him informed as to the progress of the medical social plan

The social worker has an allied responsibility to the patient to interpret the diagnosis and medical treatment to him to help him to use hospital and community resources to further his medical treatment and to

aid him in working out the personality problems which may be blocking his adjustment to a physical limitation She can function however insofar as the patient is conscious of his need and desires her help Often she sees more than one problem as she analyzes the patient s social situation but she can work only with the problem that the patient sees as the immediate one

This physician social worker relationship is necessary in clinic work As stated before the physician in rural or small urban communities has the advantage of a closer relationship to his patients and a much less complicated community organization He goes into the homes of his patients and sees them as individuals in their respective family and community groups In these instances the physician can more easily help the patients to work out their adjustments as he has ready access to community resources His personal interest in helping his patients to make adjustments and to solve the problems that hinder medical treatment is a part of the art of medical practice It can never be successfully replaced by bureaus or agencies under state control

# 24

# AN INTRODUCTION TO THE STUDY OF ELECTROCARDIOGRAPHY

## HISTORY

It has been stated that the history of any science is the science itself. Consequently there is no better means of approach to the subject of electrocardiography than a review of the steps by which it reached its present state.[96] From small beginnings in the laboratory to the ultimate perfection of an instrument of great value at the bedside the story winds through nearly 150 years. The contributions of many investigators made possible the final work of Einthoven who introduced the instrument into clinical medicine.

Electrocardiography is based upon the fundamental physiologic fact that the contraction of a muscle is accompanied by a minute electrical current. Therefore, if we desire to go back to the beginning we should examine the earliest experiments in electrophysiology. These were made by Luigi Galvani toward the end of the eighteenth century. Of course, the indefatigable John Hunter studied animal electricity in 1773 using the torpedo or electric ray fish. This peculiar property of the fish was not discovered by him, however, for we read that the Romans were aware of it and for this reason made some use of the fish therapeutically. Caldani likewise performed several experiments on the electrical stimulation of the cerebral cortex as early as 1784. However, Galvani's work, because of its completeness and conclusiveness, marks the real beginning of our knowledge.

Galvani was a distinguished professor of anatomy at the University of Bologna, and early in his career became very much interested in animal electricity. Quite by accident, in 1791, he placed a dissected frog on a laboratory table near an electric machine. It was a fortunate circumstance but the interpretation of the result had been waiting for a man of Galvani's insight and ability. As an assistant lightly touched the nerves of the frog's leg with the point of a knife Galvani observed that the muscles were thrown into vigorous contraction.

Galvani was very much interested and curious, and he was determined to find out if lightning would produce the same effect. One day during a thunder storm he dissected a frog and attached it to a conductor. He connected the feet of the frog to a wire which he grounded into the water of a nearby well. Galvani observed that

The results came about as we wished. As often as the lightning

broke forth the muscles were thrown into repeated violent contractions so that always as the lightning lighted the sky the muscle contractions and movements preceded the thunder and as it were announced its coming It was best however when the lightning was strong or the clouds from which it broke forth were near the place of the experiment

This experiment opened up a wide field for investigation Galvani later discovered that when one of his frogs was placed on a metallic plate and the hook piercing its spinal column was brought in contact with the plate a twitching occurred He repeated the experiment and in place of the metal plate he used glass and the twitching disappeared He also learned that if the frog rested on a glass plate and he touched both the nerve and the muscle with a bent rod consisting of two different metals prolonged convulsions followed In these simple experiments Galvani produced the first cell in history for generating electricity

The next advance was made by Carlo Matteucci who first demonstrated the rheoscopic frog effect (1842) In this experiment if the sciatic nerve of one leg of a frog is placed upon the muscles of the opposite leg the muscles of both legs may be made to contract by simply stimulating the sciatic nerve on the normal side The essential point for us to remember about this contribution in connection with electrocardiography is the fact that the second muscle was not stimulated directly by the current applied to the nerve but indirectly by the current of action generated in the muscle in consequence of its contraction

The time soon arrived for an application of this knowledge to the heart In 1856 Albert von Kolliker and Muller discovered that the tiny frog s heart exposed and contracting on their laboratory table produced an electric current which accompanied each beat This fact they established but at the time very little practical use could be made of it because of the crude apparatus available for additional investigation

It was not until 1878 that further progress was made by two English physiologists Sanderson and Page These workers successfully recorded for the first time the minute heart current described by von Kolliker and Muller by means of the capillary electrometer This instrument consists of a column of mercury in a vertical glass tube the end of which dips into sulfuric acid These investigators noted that if an electric current no matter how small disturbs the relation between the mercury and the acid the slender column of mercury moves to a new position in the tube This response of the mercury column to the electric current was photographed by Sanderson and Page on a moving sensitive plate

However even the physiologists found that the capillary electrometer was a delicate temperamental instrument It was no easy task to make it operate successfully and at times it must have sorely tried the patience of the laboratory workers Then too the hearts under investigation had

to be connected directly to the instrument which made the study a matter of laboratory interest only

In 1887 Waller made the important discovery that the heart s currents could be demonstrated without opening the chests of the laboratory animals He merely connected the outside of the body to the capillary electrometer by electrode These wire connections were later to become known as 'Leads ' Waller immediately applied this idea to man and found that here too the delicate heart current could be led off the arms and legs of his subjects

So far in our survey we see that the scientists had shown a small current to be present when the heart contracted they had found a way to measure it crudely and Waller showed that the current could be led off the arms and legs of the subject However, the troublesome capillary electrometer remained The acid and the mercury had their faults and shortcomings The mercury possessed inertia and the curves of its movements, when photographed were not true curves The hard pressed physiologists had to correct their experiments for the mercury inertia by mathematical computations Surely the practitioner of medicine could not be expected to carry out such work so this valuable method of study had to remain in the laboratory

The years were quickly passing and the century was almost spent Many discoveries of more dramatic and of a more practical nature were taking the attention of the physicians New germs were being described antisepsis was coming into vogue in fact medical discoveries were pouring in on the bewildered doctors from all quarters with the rapidity of corn popping in a pan Consequently the progress made in the registration of the heart s current remained far below the clinical horizon

With the turn of the century the man destined to bring the method out of the shadow arrived on the scene The year was 1903 the place Leyden Holland the man Willem Einthoven whose final contribution made electrocardiography a clinical reality His work enabled scientists to discard the capillary electrometer and use in its place for recording the heart s current the much more rugged and reliable string galvanometer This instrument had already been invented by J S C Schweigger of the University of Halle but Einthoven perfected it and applied it to the measuring of the electric current generated by the heart s contraction

He found that the delicate quartz string contained in the galvanometer moved more quickly and did not have the lag of the mercury This observation gave us at last a practical method of electrocardiography With Einthoven s use of the galvanometer in place of the capillary electrometer the journey of the method from the laboratory to the bedside took just a few years The scientific study of diseases of the heart then began in earnest

The original apparatus of Einthoven was very large and cumbersome The magnet was of considerable size and the string that was mounted be

tween its poles was an intricate mechanism The original instruments took up considerable space and the details of their operation discouraged the ordinary clinical worker For this reason few hospitals had electrocardiographs prior to 1905 06 About this time Sir Thomas Lewis began to use the electrocardiograph in England and the popularity of the method at the end of the first decade of the present century was largely a result of his efforts As the century grew older the instrument was simplified and more and more was learned of its usefulness The improved instrument was made to occupy less space in the laboratory until more compact and easily portable electrocardiographs for bedside work became a reality

Today the clinician leans heavily on the electrocardiograph In some cardiac conditions a tracing is essential before a final diagnosis can be made Moreover the electrocardiogram tells a great deal concerning the progress of patients and guides the administration of certain drugs Its future is bright The tiny current produced by the frog s heart in van Kolliker s laboratory in Wurzburg in 1856 opened up a large field for scientific study and research which is broadening year by year The ultimate extent of its progress is a matter of pure conjecture as new depths are being plumbed and new uses are being discovered for the method by clinicians as well as by laboratory workers

## THE APPARATUS

Let us now examine the essential features of the modern electrocardiograph (Fig 164) The lamp (L) sends a beam of light through a condens-

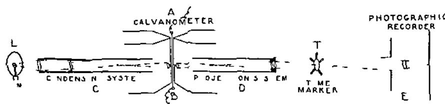



Fig 164 A simplified diagram showing the essential parts of an electrocardiograph of the string galvanometer type See text for description

ing system (C) This is focused on the galvanometer string (A B) stretched in an electromagnetic field between the poles of two powerful electromagnets When the heart current of the patient is passed through this fine quartz string the string moves across the gap at right angles to the lines of magnetic force and its shadow is magnified as it passes through the projection system (D) and falls on the moving strip of film in the camera at E At T a time marker interrupts the beam of light at intervals of 0 04 second and these vertical markings appear on the developed strip of film (Fig 165) This is the principle of the instruments that contain a string galvanometer For a more detailed description of the construction of the

various types of electrocardiographs the reader is referred to the special texts on the subject[6, 7]

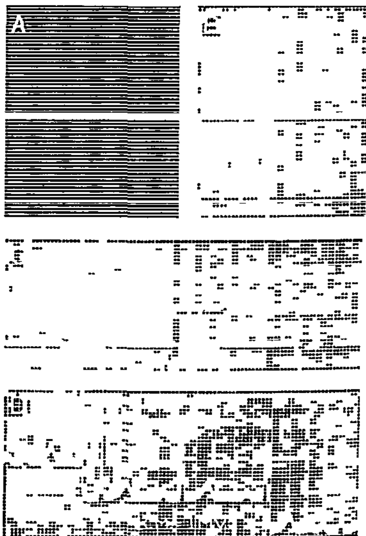



Fig 165 A Shadow of the string The time marker is not running B Same with the time marker running Note the presence of vertical lines that indicate the time markings C Standardizing string tension before introducing the patient into the circuit. Note the deflections of the string caused by one and two millivolts D Normal electrocardiogram (Lead I) Note the standardization The introduction of 1 mv deflects the string exactly one cm

In the early days a very large room in the hospital was assigned to the Heart Department to accommodate the equipment Electrocardiographs were big and cumbersome repairs were difficult and a finished record was

an achievement Today most models are rugged easily operated by a technician and seldom present the mechanical difficulties that made the early workers in this field true pioneers Figure 166 shows a model in common use today A glance will show the general principle of its construction since its various parts are designated by the same letters used

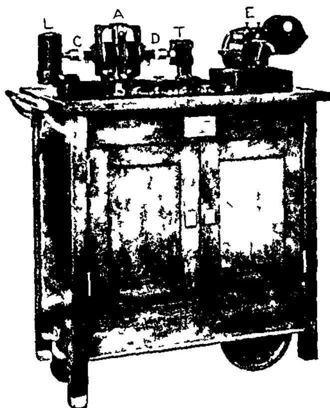



FIG 166 Modern mobile type electrocardiograph containing string galvanometer The letters correspond to those of Fig 164 (Courtesy Cambridge Instrument Co)

in the schematic drawing Recently smaller more compact models that can be *readily carried to the bedside of the patient have been perfected* (Fig 167)

There is a difference in the construction of some of these instruments that deserves mention Perfection of the amplifier tube has made it possible to magnify many times the current derived from the patient This permits the use of a less delicate galvanometer Instead of photographing the motions of the string these newer instruments record the motion of a beam of light reflected from a mirror contained in the

galvanometer (Fig 168) At present there are several models on the market that employ this principle They are small, serve readily at the bedside and appear to be as suitable as the original models containing the more delicate string galvanometer The electrocardiograms obtained from the two types of instruments are identical, the amplification of the heart current apparently does not distort the individual waves A recent addition to the electrocardiograph that has appeared is a compact system for recording the heart sounds simultaneously with the electrocardiogram (pages 23 584)



Fig 167 A bedside tracing using portable model electrocardiograph (Courtesy Children's Heart Hospital and Cambridge Instrument Co )

An addition to one of the amplifying types of electrocardiographs recently placed on the market is the "Cardioscope" This attachment makes possible the reproduction of the image of the electrocardiogram on a moving fluorescent screen or drum (Fig 169) The electrocardiogram can be seen by looking through the window of the instrument and the reading may be made at once Time and amplitude lines are thrown on the screen when desired by means of a switch The Cardioscope makes it possible to secure a constant viewing of the heart's action during the course of a long surgical operation or animal experiment and consequently saves considerable film A tracing however may be recorded at any time if the physician detects an interesting event in the electrocardiogram on the moving drum In cases of suspected coronary occlusion this instrument also

FIG 168 Diagram illustrating principles of electrocardiograph of the vacuum tube type The current from the patient passes through amplifier (1) and then to a galvanometer of special design ( ) The galvanometer contains a mirror which reflects a beam of light from source (3) As the galvanometer responds to the amplified heart current it causes the beam of light to move across the film in the camera (5) (Courtesy General Electric Co )

FIG 169 The cardiscope (Courtesy Sanborn Company )

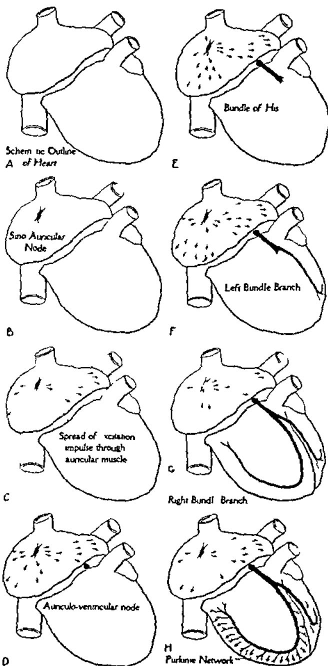



Fig 170 Schematic diagrams representing component parts of the con luct on system of the heart See text for explanation

enables the investigator to note the electrocardiogram obtained by using various points of contact on the chest wall and to record on the film only the complexes that appear to be most useful in the diagnosis

## PHYSIOLOGIC PRINCIPLES

The chambers of the heart contract in sequence following an excitation wave that passes down the specialized tissue of the conduction system (Fig 170) The impulse for cardiac contraction originates in the sino

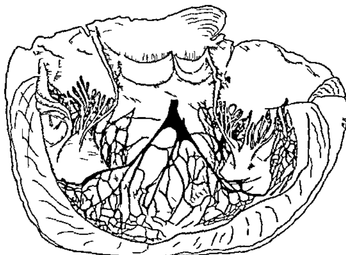


FIG 171 India ink injection of beef heart showing the conduction system

auricular node (synonyms sinus node the Keith Flack node the S A node the pacemaker) This is a vascularized island of special tissue situated high up on the posterior wall of the right auricle (B) The impulse passed from here into the muscle of the auricle There is no special pathway for conducting this impulse through the auricular musculature consequently the wave spread equally in all directions (C)

Another clump of specialized tissue the auriculo ventricular node (synonyms A V node node of Aschoff and Tawara), next receives the impulse (D) From here it travels down the bundle of His (E) and is distributed equally to each ventricle through the right and left branches of the bundle (F and G) finally arriving at the terminal *ramifications of* the system the Purkinje network (H) lining the inner ventricular wall The spread of the impulse is now complete

Although the human heart does not lend itself readily to a demonstration of this conduction system the ox heart with the proper technic and a little patience may be injected to show the entire system If the fresh

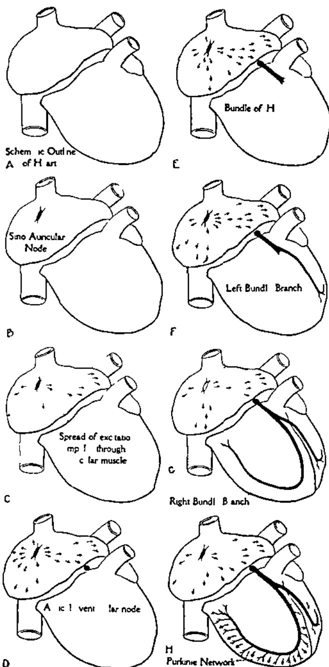



Fig 170 Schematic diagrams representing component parts of the conduction system of the heart See text for explanation

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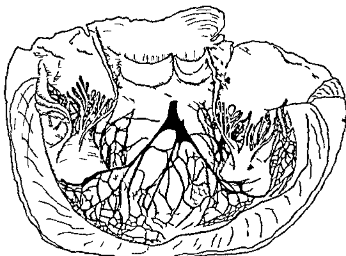


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Although the human heart does not lend itself readily to a demonstration of this conduction system the ox heart with the proper technic and a little patience may be injected to show the entire system If the fresh

ox heart is allowed to stand for 12 hours at room temperature the slight shrinkage that follows early degeneration about the specialized conduction tissue will permit the passage of injection fluid The needle of a syringe containing 5 cc of India ink is then inserted into the upper part of the

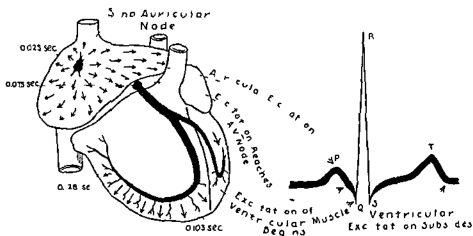



FIG 17 Diagram illustrating relationship between the spread of the excitation impulse and the electrocardiogram The figures represent the time intervals

bundle A slight amount of pressure forces the ink along this dead space, and the whole conduction system will be strikingly outlined (Fig 171)

The waves of the electrocardiogram are produced by the spread of the excitation impulse and are in no way related to the strength of the ensuing cardiac contraction These waves were originally named by Einthoven

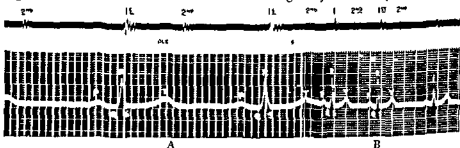



FIG 173 Sound tracing and electrocardiogram simultaneously recorded by Sanborn Stetho cardiette A Speed of paper 75 mm per second B Speed of paper 75 mm per second (Courtesy Sanborn Company)

in purely empirical fashion P Q R S and T Figure 172 shows the relationship between the spread of the impulse and the electrocardiogram As the electrical excitation passes through the auricular muscle the P or auricular wave is inscribed in presystole The string then returns to the base line With the upstroke of the R wave the auricular cycle (or auricular complex) ends The ventricular cycle (or complex) usu

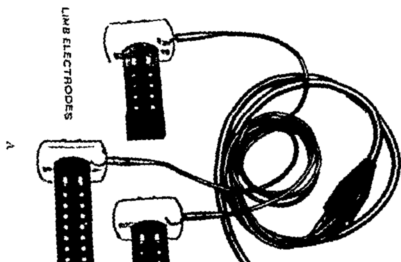



Fig 174 A El ctrod for d rect and ind t l t ls B Electro les n p lac

ally opens with a small initial downward dip of the string or Q wave, followed by an upward R wave Again the string returns to the base line At this point a small dip below this level may be observed This downward deflection is the S wave A broad blunt upright wave is next inscribed, this is known as the T wave Rarely, an additional smaller, and usually unimportant wave may follow the T wave This is known as the U wave and is produced by the events of early diastole (see Fig 175)

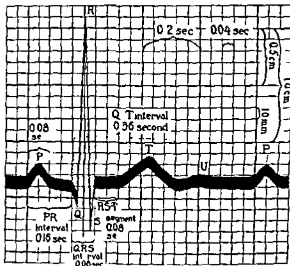



FIG 175 The electrocardiogram single lead (From Essentials of Electrocardiography Ashman and Hull Macmillan Company N Y )

In Fig 173 we will see the relationship between the electrocardiogram and the heart sounds of a normal subject Note that the peak of the R wave is recorded before the first sound of the heart is heard at the apex The second sound of the heart immediately follows the T wave

As previously stated any two parts of the body with the heart between them may be chosen as points of contact for leading the current of the heart from the body These leads are three in number and for convenience the arms and the left leg are used The waves of the electrocardiogram vary in relation to the location of the electrodes on the body surface Lead 1 is obtained by placing the German silver electrodes on the arms (Fig 174) This is usually done by rubbing the skin at the point of contact with a small amount of a special jelly Lead 2 represents the curve obtained when the current passes through the string galvanometer from the right arm to the left leg and lead 3 results when the left arm and the left leg are connected Using three leads in each case gives a better tracing of cardiac events than any single lead Additional precordial leads are obtained by placing the electrodes directly on the chest These special direct leads will be considered in detail later (page 637)

## THE ELECTROCARDIOGRAM

We will now turn our attention to a study of the details of the electrocardiogram First of all it should be noted (Fig 175) that the smallest squares in the blocks represent 0 04 second in the horizontal direction In the vertical direction each block represents a potential difference of 0 1 millivolt Note that the string moves over ten of these small squares when the operator throws one millivolt into the circuit (see Fig 165) In other words each electrocardiogram is standardized so that ten small blocks in the vertical direction (or 1 cm ) equal a potential difference of one millivolt Consequently in all electrocardiograms no matter where they are taken the voltage of the waves can be determined accurately The voltage or amplitude of all waves is measured from the top of the base line to the top of the deflection If we are dealing with a downward deflection we measure from the bottom of the base line to the lowest point of the deflection The duration of the waves and intervals can be accurately measured on the horizontal base line

## TECHNICAL FAULTS

For detailed technical data concerning the recording developing and filing of the electrocardiograms the reader is referred to one of the special

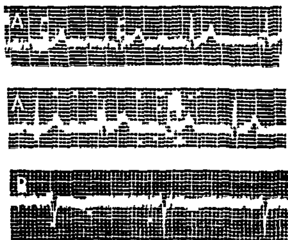



Fig 176 Artefacts in the electrocardiogram caused by A Nervous patient (not relaxed) Middle strip (A) and last strip (B) show improper elimination of electrical interference in vicinity of patient

treatises on the subject However the physician should become acquainted with a few details of the technic that have a direct bearing on the form of the record he receives A laboratory report of any kind to be of clinical

value must be the work of a careful and skilled technician The electro cardiogram is no exception to this rule

The room in which the tracings are taken should be quiet and apart from the main thoroughfare of hospital or office It should be kept com fortably warm in the winter and should have no telephone connections

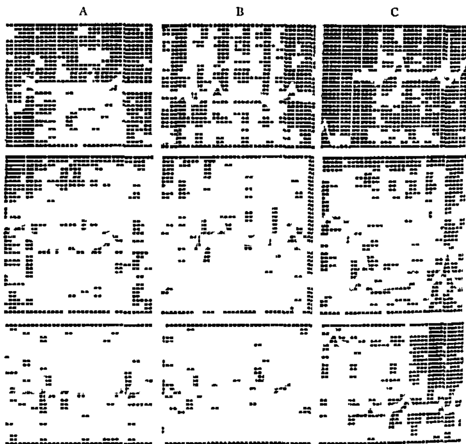



Fig 177 Electrocardiograms of the same patient showing variations produced by differences in string tension One millivolt is introduced in each instance A String too tight The deflection is only 0 5 cm B String tension correct One mv deflects the string one cm C String too loose The millivolt deflects the string 1 5 cm

The patient should be allowed to lie down and relax for a short time before the tracing is taken and the bed or table should be comfortable Conversa tions with the technician while the record is being taken should be avoided These points are all essential for the production of good electrocardiograms

The mental reactions of the patient may often cause variations in the skin current with the production of artefacts in the base line Movements of the patient during the examination or even the tension of the muscles resulting from an uncomfortable position naturally affect the electro-

cardiogram (Fig 176) Electric appliances in the vicinity may cause fuzziness of the string shadow although interference of this type can be eliminated satisfactorily in the modern instruments Quite marked artefacts in the record may occur if the skin resistance is too high because of haste on the part of the technician in preparing the patient for the examination This may result in over shooting of the deflection when one millivolt is introduced If the electrocardiogram is taken before this is corrected the waves will be too large and after each quick deflection the string will overshoot the zero level If the standardization is not exact the voltage of the waves will be incorrect (Fig 177) When electrocardiograms are taken with the patient in recumbency all subsequent records used for comparative study should be taken in a similar position since change in position produces alterations in the form of the electrocardiogram (Fig 178)

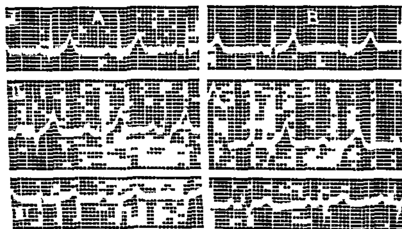


FIG 178 Electrocardiograms taken on the same person showing the effect of change in position A patient sitting upright in a chair B patient recumbent

## THE P WAVE

The P wave is the first wave of a group of deflections that makes up the electrocardiogram It precedes the QRS group and represents auricular activity Normally the P wave is a round upright deflection measuring not more than 0 1 second and averaging 1 to 2 mm in height In lead 3 of the electrocardiogram the P wave may be upright isoelectric (buried in and not projecting above the base line) or inverted (projecting below the base line) (Fig 179) If the rate of the heart is rapid the P wave may fall upon the downstroke of the preceding T wave In severe tachycardia the P wave may be lost within the T wave making the reading of the tracing difficult The P wave reappears however with the onset of a slower cardiac rate

## The P-R (P-Q) Interval

One of the most important measurements in electrocardiography is the time interval (measured on the base line) from the beginning of the P wave to the initial deflection of the QRS complex. This is known as the P-R interval and indicates the time consumed in the passage of the impulse from the S-A node to the ventricular muscle. It averages 0.15 second in the normal adult and should not exceed 0.20 second. It varies with body size and cardiac rate. With increase in the cardiac rate, there is a slight decrease in the P-R interval.

## The QRS or Ventricular Complexes

The Q, R, and S waves of the electrocardiogram represent ventricular activity. The first deflection is downward and is known as the Q wave. It is often absent in normal individuals. The next deflection is upward and is known as the R wave. The descending limb may dip below the base line forming an S-wave. The exact form of these waves in each lead is determined by the direction that the excitation wave pursues through the ventricular muscle. In some cases where several waves of low voltage compose the QRS group, it is referred to as a W-shaped or an M-shaped QRS complex. A difference in the direction of the waves of the QRS group may be caused by a change in the heart's position, pregnancy, an abdominal tumor, high diaphragm or ascites. The height of the QRS is generally between 5 and 20 mm. (0.5 to 2.0 mv.). If over 20 mm., the QRS group is spoken of as showing "high voltage"; if below 5 mm., it is said to have "low voltage." The duration of the QRS group should not exceed 0.1 second. However, in the presence of cardiac hypertrophy a longer time will be necessary for the impulse to pass through the thickened heart wall; consequently the QRS interval is apt to be prolonged slightly. The QRS may normally show notching or low voltage or both in lead 3.

## The T-Wave

The T wave represents the retreat of negativity from the ventricular muscle. Normally it is upright and measures between 0.15 and 0.5 millivolt and should not exceed 0.25 second in duration. Significant and important changes in the T wave will be described later in relation to a number of cardiac conditions. The T wave in lead 3 may be normally flat or inverted and occasionally, under some circumstances, the T waves in leads 2 and 3 may show a similar alteration in normal individuals. Such changes in $T_1$ are usually indicative of cardiac damage. The T wave amplitude may be high in children following exercise, in thyrotoxicosis or for no apparent reason. In older patients the T wave amplitude tends to decrease.

### The Q T Interval

The Q T interval is measured from the beginning of the QRS complex to the end of the T wave and represents ventricular systole It varies with the cardiac rate showing increase with slow cardiac rates and decrease with a rapid rate While there is still much to be learned about the importance of this measurement it should always be studied carefully, especially in patients who have evidence of myocardial infections or chemical imbalance

### The RS T Interval

The RS T interval is the measured distance between the last QRS deflection and the upstroke of the T wave It is important to note whether this segment is raised above or depressed below the base line Distances exceeding 0 1 millivolt in either direction are abnormal The average duration of the RS T interval is from 0 24 to 0 28 second

### Alterations in the Waves of the Electrocardiogram and Their Significance

#### P wave changes

When the P wave is notched inverted or higher than 2 5 mm it may be said to be abnormal In mitral and pulmonary stenosis structural alterations are observed in the auricular musculature and these may be reflected in the P wave of the electrocardiogram Notching and increase in the duration of the P wave beyond 0 1 second are common changes in mitral disease Care must be used however in interpreting slight alterations If the notching of the P wave is slight and occurs in leads 2 and 3 the finding should not be stressed If the notching is marked and occurs in lead 1 it is significant A normal upright P wave appears in the electrocardiogram when the impulse originates in the sinus node Should the impulse for cardiac contraction arise in any area outside the sinus node or pacemaker we may expect to find an inversion or alteration in size and shape of the P wave The P waves of auricular premature contractions for this reason are often quite different from the P waves of the rest of the tracing The alteration in form of the P wave is usually proportional to the distance of the ectopic focus from the pacemaker (Fig 179 G) When a part of the P wave appears above the base line and a part below this level it is said to be diphasic (Fig 179 E) Diphasic or inverted P waves also occur in paroxysmal tachycardias of auricular origin Here the abnormal focus of impulse formation instead of initiating a single contraction for a time becomes the pacemaker and sends out impulses at a rate usually exceeding 160 per minute Other parts of the conduction system may become more excitable and initiate impulses for cardiac contraction In such a case the impulse may spread backward (retrogression) and produce auricular contraction This may occur before

during or after the ventricular contraction, depending on the site of formation of the new impulse If auricular contraction follows that of the ventricle the P wave will appear following the QRS instead of in the usual location, and it will usually show inversion As we will see later there are no P-waves when auricular fibrillation is present Occasionally the sinus node may fail to generate an impulse or the auricles do not respond to the sinus impulse for the space of one or more cardiac cycles this is known as sinus arrest The P wave and consequently all the other waves of the cycle are absent (Fig 180 A and B)

### ABNORMAL P R INTERVAL

Prolongation of the P R interval over 0 20 second is distinctly abnormal and points to auriculo ventricular block (Fig 181) It may accompany



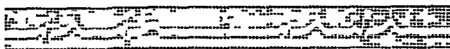
Fig 179 Abnormalities of the P Wave A normal B flat C pointed D widened; E notched and widened F inverted G a change is seen from upright to inverted caused by shift in site of impulse formation

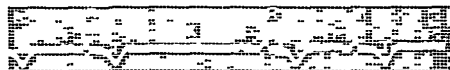
diphtheritic carditis and is one of the most valuable signs in the presence of acute myocarditis Over 25 per cent of patients show prolongation of the P R interval during active stages of a rheumatic infection In many of these cases an overactivity of the vagus may be a contributing factor Increase in the P-R interval may be caused by defective conduction following interference with the blood supply to the bundle of His Consequently arteriosclerotic (rarely syphilitic) heart disease may produce this alteration

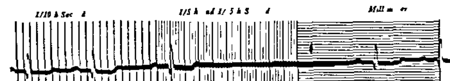
### CHANGES IN THE QRS COMPLEX

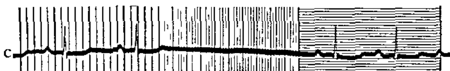
It is important to remember that an impulse for cardiac contraction arising anywhere above the bundle will result in the normal spread of the excitation wave and produce a QRS complex of normal configuration Occasionally the distribution will be abnormal and a slight difference in the QRS complex results these beats are called aberrant

When we examine the QRS complex the following points must be noted









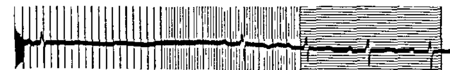



FIG 180 Sinus arrest In A and B note omission of one complete cardiac cycle In C there are two complete cycles omitted from each lead (See Case No 66)

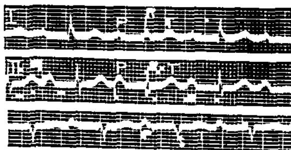


FIG 181 Prolongation of the P R Interval or first stage heart block In lead  the P R Intervals measure 0 3 second (See Case No 36)

the direction of the major deflection (particularly in leads 1 and 3) the duration the configuration and the height Notching in lead 3 alone cannot be considered as an abnormal finding However, notching in leads 1 and 2 (particularly the M and W shaped complexes) must be considered as evidence of myocardial disease A slight notching seen near the base line is not as important as that observed at the top of the R wave (Fig 182) All low voltage QRS groups occasionally show notching in the absence of myocardial damage Marked notching of the QRS is seen in premature beats and in bundle branch block These departures from the

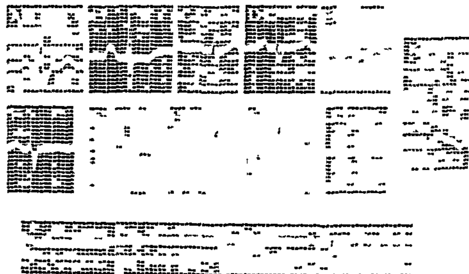


Fig 182 Variations in configuration of the QRS group A normal B diphasic C low voltage D notched (W shaped complex) E diphasic and slurred F shaded with deep S wave G slightly widened, notched and low voltage H slurred with deep S wave I widened and notched (bundle branch block) J deep Q wave in lead 3 K high voltage L respiratory variations in QRS amplitude in lead 3

normal will be considered in detail later Low voltage of the QRS sometimes occurs in patients with extensive edema hypothyroidism constrictive pericarditis and myocardial weakness The latter is the explanation of the low voltage electrocardiogram that often follows occlusion of the coronary arteries Low voltage QRS may be present occasionally in the absence of heart disease Consequently a low voltage electrocardiogram can be interpreted correctly only in the light of the clinical findings

The duration of the QRS group should not be more than 0 1 second when it exceeds this myocardial disease should be suspected unless one of the usual types of bundle branch block is present Normally the QRS is tallest in lead 2 consequently increased amplitude in this lead as a single finding has no significance The direction of the QRS groups in leads 1 and 3 is important in determining the axis deviation (page 597)

CHANGES IN THE RS T INTERVAL

Changes in this area between the end of the QRS and the beginning of the T wave have considerable clinical significance Elevation or depression of this segment in relation to the base line should always be carefully noted Digitalis may cause a marked alteration in this area Characteristic deformities also occur in the presence of coronary occlusion Both will be considered in detail later

CHANGES IN THE Q-T INTERVAL

The distance between the first part of the QRS and the end of the T wave can be said to correspond approximately to ventricular systole

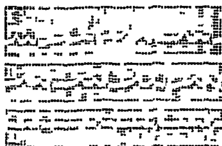


FIG 183 Prolongation of the Q T Intervals in hypocalcemia

and is lengthened in hypocalcemia (Fig 183) and after emergence from diabetic coma

CHANGES IN THE Q-WAVE

Recently a deep Q wave in lead 3 particularly when accompanied by a Q wave in lead 2 and an inversion of $T_3$ has been shown to be a

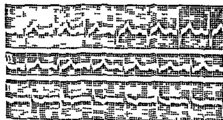


FIG 184 Deep Q wave in lead 3 In this instance it accompanied pregnancy and disappeared after delivery

significant electrocardiographic finding It often follows a posterior coronary occlusion On the other hand a deep $Q_3$ may accompany pregnancy (because of the high diaphragm) and disappear following delivery

(Fig 184) Here again correct interpretation of the electrocardiogram depends on a knowledge of the clinical findings If the history and physical examination are negative too much significance should not be attached to the isolated finding of a deep Q wave in lead 3 However, it always warrants a further study of the patient (see Figs 237 243 247)

T WAVE CHANGES

Inversion of the T wave particularly in lead 1 is significant The shape of the T wave and type of deformity in each instance are the important



FIG 185 Variations in the T wave A normal B large amplitude C diphasic D flat E inverted F deeply inverted (coronary type with deep Q)

factor For example it will be readily seen that the type of the T wave inversion differs in Fig 185 E and F from that observed in Fig 250 In the change of the T wave from its normal upright position to inversion a stage in the development is flattening Consequently flattening of the T-wave is an important observation particularly when it occurs in lead 1 However in some hearts particularly of the long ptotic or drop type too much significance should not be attached to this change If the T wave in lead 1 is low with upright and normal $T_2$ and $T_3$ in a person of this build it should be considered normal This again demonstrates that the decision regarding the exact meaning of an electrocardiographic alteration can be made only when the result of a complete examination of the patient is known This is particularly true in cases on inversion of the T wave in lead 3 It has been said that a slight degree of inversion of $T_3$ is normal Deep inversion however should arouse suspicion since this abnormality may follow a posterior coronary occlusion (Fig 185 F) This electrocardiographic finding particularly if accompanied by a deep $Q_3$ and inverted $T_3$ should direct attention to the past history of these patients and inquiry should be made concerning the presence of chest pain slight or severe *in degree* at some previous time

THE ELECTRICAL AXIS AND ITS DEVIATION

Change in the electrical axis of the electrocardiogram is important The axis may deviate to the right or to the left Although a complete study of axis deviation may prove complex even to the initiated, the main principles should be readily grasped Let us suppose that the solid arrow A B in Fig 186 A represents the value and direction of the various action currents generated in the heart as it contracts If lines are drawn perpendicular to the three sides of an equilateral triangle CED (representing the three leads of the electrocardiogram), the values of $a_1b_1$, a b and $a_3b_3$ will represent the values of the QRS in each lead (Fig 186 B) It

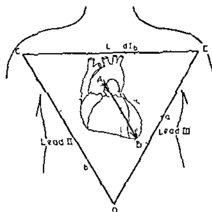



FIG 186 A Einthoven's triangle See text for explanation

will be readily seen that if the heart changes position in the chest and rotates to the right and assumes the position of the dotted arrow in the diagram the value of $a_1b_1$ will decrease When the arrow representing the action curve is exactly perpendicular to the base of the triangle the QRS voltage will be zero Should the rotation of the heart take place still further to the right the tip of the arrow will move toward the side CD and the current represented by the projections of the new position of the heart will flow in the opposite direction—and the QRS in lead 1 will now be inverted instead of upright Right axis deviation is then said to be present (Fig 187 A) A similar rotation of the heart to the left will bring the arrow A B perpendicular to the side DE In this position the value of the QRS in lead 3 will be zero Should the displacement be more marked and the point of the arrow move farther to the left the direction of the current as plotted on the side DE will be reversed Left axis deviation will then be present (Fig 187 B)

**Rule** Left axis deviation is present when the major deflection is upward in lead 1 and downward in lead 3 Right axis devia

tion is present when the major deflection of the QRS is downward in lead 1 and upward in lead 3 When the QRS complexes

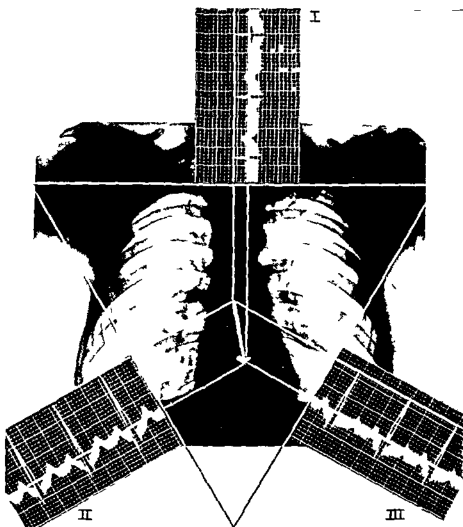



Fig 186 B Illustrates diagrammatically the effect of a transverse position of the heart on the size and direction of the main deflections of the electrocardiogram An Einthoven (equilateral) triangle is drawn about the heart The arrow represents both the electrical and anatomical axes of the heart The size and direction of the R wave in each lead is obtained by vertical projection of the ends of the arrow on that lead (From Master A M The Electrocardiogram and X Ray Configuration of the Heart Courtesy Lea and Febiger Co Phila )

are upright in leads 1 and 3 no axis deviation is present With no axis deviation QRS is higher than either $QRS_1$ or $QRS_3$ With either right or left axis deviation, it is lower

Axis deviation is generally interpreted as meaning preponderance of the right or left side of the heart Consequently in clinical conditions affecting the left side of the heart, such as hypertension aortic regurgitation

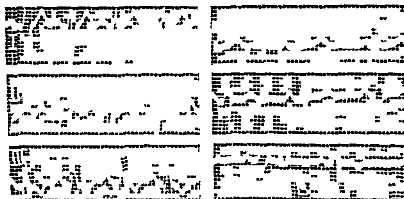


FIG 187 A Right axis deviation B Left axis deviation

FIG 188 Normal electrocardiograms showing variations at different age periods

or aortic stenosis left axis deviation is commonly encountered Similarly in mitral stenosis with enlargement of the right ventricle some degree of right axis deviation may be expected in the electrocardiogram It can also be seen that IF EXTREME HYPERTROPHY OF THE HEART IS PRESENT AF

FECTING THE TWO SIDES EQUALLY WITH THE INITIAL RATIO UNDISTURBED THE ELECTRICAL FORCES WILL BALANCE AND NO AXIS DEVIATION WILL RESULT

Outside influences changing the position of the heart in the thorax may produce axis deviation A high diaphragm resulting from pregnancy or abdominal tumor or a large pleural effusion in the right chest may rotate the heart to the left and produce a left axis deviation Occasionally as the relationship between the mass of the left ventricle and the right ventricle changes in normal hearts, an axis deviation may result For example at birth and for the first few weeks of life, the mass of the right ventricle ex

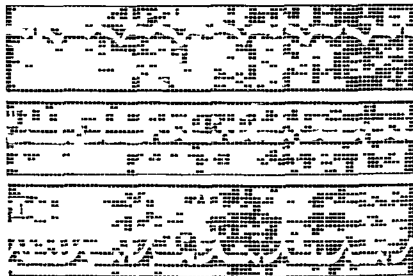


FIG 189 The electrocardiogram in dextrocardia Note inversion of all waves in lead I

ceeds that of the left and right axis deviation is seen (Fig 188) In the older age groups the relationship is in favor of the left ventricle consequently left axis deviation may appear as a normal finding

If we view the heart under the fluoroscope we will note that in some cases there is a marked change in its position following deep inspiration This amount of alteration in cardiac position can cause a shift in the electrical axis of sufficient degree to be recorded in the electrocardiogram (see Fig 182 L) If the respiratory excursion is slight or if the heart rests lightly on the diaphragm as it does in ptotic individual the change in cardiac position will be scarcely noticeable and there will be no alteration in the tracing

Congenital dextrocardia presents a characteristic electrocardiographic picture (Fig 189) All the waves in lead I are inverted This is what we would expect since the heart in these patients is opposite in its relationship to the leads A similar electrocardiographic picture results if the lead cords to the patient s arms are reversed by a careless technician

## READING THE ELECTROCARDIOGRAM

Before a detailed interpretation of the electrocardiogram is attempted a resume of all the clinical data available at the time of the examination should be in the hands of the physician giving the report If this rule is followed in every case many errors in the clinical application of electrocardiography will be avoided A suitable form covering all essential details is shown in Table XXIV Before the tracing is mounted for study make certain that the standardization is correct i e a string deflection of 1 cm follows the introduction of one millivolt potential difference (see Fig 165 C and D) Suitable seven inch strips should then be selected from each lead for mounting either in the elaborate (and more expensive) forms issued by the instrument companies or on a sheet of ordinary paper the size of the ward chart

TABLE XXIV

HOSPITAL OF
THE WOMAN S MEDICAL COLLEGE OF PENNSYLVANIA
DEPARTMENT OF CARDIOLOGY

REQUEST FOR 1—ELECTROCARDIOGRAM
2—ORTHODIAGRAM Check examination
3—CLINICAL OPINION desired

(Note Requests for electrocardiograms should be made in all cases where the clinical condition warrants and should be signed for by the chief of the service)

NAME Ward Out Patient Semi Private Private
Age (Please check status)
Date Service of
Blood Pressure Height Weight

RÉSUMÉ OF THE CLINICAL FINDINGS (Include your impression of the etiology heart size and rhythm)

CLINICAL DIAGNOSIS
HAS PATIENT RECENTLY RECEIVED DIGITALIS MORPHINE OR QUINIDINE? IF SO HOW LONG AND IN WHAT QUANTITIES?
ADDITIONAL LABORATORY DATA (Include here urinalysis blood count blood chemistry and serology)

—————————————— M D

NOTE It is most important that above form be completely filled out in order that proper interpretation of laboratory data can be made With frequent requests (serial studies) only details of progress and additional laboratory studies need be furnished

In order that all the features of the electrocardiogram may be included in the description it is well for the beginner to adopt a definite method of procedure and follow it in all subsequent studies Important items are then not likely to be overlooked First note the rate of the heart This may be determined by placing a six inch ruler (usually equivalent to 30 of the fifth of a second divisions) beneath the strip of film and counting the number of auricular and ventricular cycles included in this measurement In Fig 190 the rate is 80 normal sinus rhythm is present and each auricular

wave (P) is followed by a ventricular complex (QRS) The rhythm is carefully studied by noting the presence of P waves their position in the cycle and the distance between them With a pair of architect's dividers span the distance between the peaks of the QRS complexes In Fig 190 it will be seen that they are equidistant The rhythm therefore, is regular, and the P waves show that it is of sinus node origin Next note the size shape and duration of the P wave in each lead In Fig 190 $P_1$ is widened measuring 0 12 second In lead 2 the P-waves are peaked, while in lead 3 they appear to be diphasic The P R intervals (measuring from the

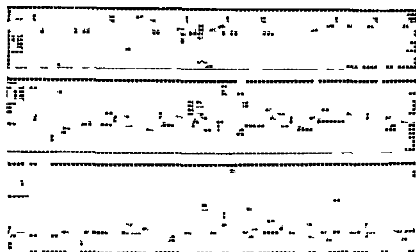


Fig 190 Electrocardiogram of a woman of 34 admitted to the hospital because of increasing dyspnea edema and hemoptysis She gave a history of two attacks of rheumatic fever in childhood Examination showed cardiac enlargement presystolic and diastolic apical murmurs and an accentuated pulmonic second sound Tablets of the whole leaf of digitalis 0 1 Gm (gr 1½) had been given after meals for three days prior to admission See text for reading

beginning of the P wave to the first deflection of the QRS) are 0 20 second in duration in lead 2 There is present a deep S wave in lead 1 The QRS in lead 2 has an R wave and a small S wave and is diphasic The T wave in lead 1 is upright and normal In lead 2 there is a depression of the S-T interval The same is present to a more marked extent in lead 3 *Right axis deviation is seen (inverted QRS in lead 1 and upright in lead 3)*

**Summary** Prominent and widened P or auricular waves, right axis deviation and depression of the S T intervals in leads 2 and 3

**Clinical Conclusions** The P wave changes and the right axis deviation support the diagnosis of mitral stenosis and suggest the presence of hypertrophy and disease of the auricular muscle and right sided cardiac enlargement The depressed S T intervals in leads 2 and 3 show beginning digitalis action

## SINUS MECHANISMS

If impulses arise from the sinus node at a rate of 60 to 100 per minute the P waves will have a normal shape and the cycles in the electrocardiogram will be equally spaced This is spoken of as normal sinus rhythm

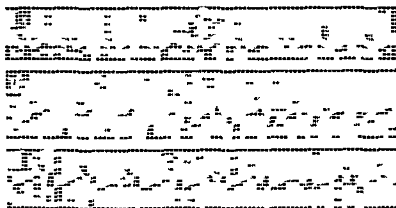


FIG 191 Electrocardiogram of a woman of 40 who showed all the clinical signs of thyrotoxicosis The basal metabolic rate was plus 55 per cent Rate 150 Sinus tachycardia

If the sinus node initiates impulses at a rate exceeding 100 per minute sinus tachycardia is present These impulses all follow the normal pathway A glance at the tracing (Fig 191 lead 1) shows that all the waves of the electrocardiogram (P QRS and T) have a normal relationship The in

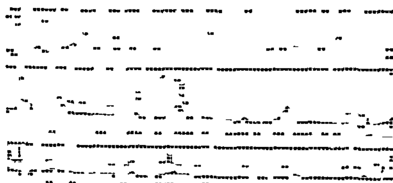


FIG 19 S nus b adyc rd a (Rat 58) Note that the intervals between the T wave and the follow n P wave a e prolonged

terval between the end of the T wave and the next P wave is shortened In lead 2 this T P interval is so decreased that the P wave arises from the downstroke of the preceding T wave

When the rate of impulse production is less than 60 per minute sinus bradycardia is present In Fig 192 the cardiac rate is 58 All the waves of the electrocardiogram appear to be normal, but the distance between the end of the T wave and the next P-wave (ventricular diastole) is prolonged Note the low voltage and notching of QRS in lead 3 THIS IS NOT AN ABNORMAL FINDING WHEN IT OCCURS IN LEAD 3 ALONE No abnormalities could be detected in the cardiovascular system of this patient The tracing was taken during convalescence from influenza

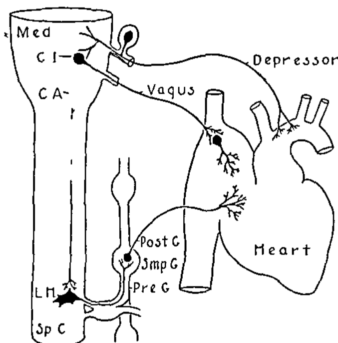



FIG 193 Diagram illustrating innervation of the heart

Although the initiation and transmission of the cardiac impulses do not depend upon the nervous system the activity of the heart is controlled by extrinsic nerves The vagus and sympathetic (Fig 193) are regulators of cardiac action increasing and decreasing cardiac rate according to the bodily needs of the moment The vagus sends fibers to the auricle and slows the heart through its influence on the sinus node and auricular muscle In youthful subjects who have normal hearts there may be noted a slowing down and a speeding up of cardiac rate during inspiration and expiration Inspiration speeds the rate while expiration slows the rate This irregularity is known as juvenile arrhythmia sinus arrhythmia or vagal arrhythmia and is caused by alterations in the vagal tone In some instances where the respiratory relationship is absent the arrhythmia may be caused by digitalis Figure 194 shows a marked sinus

arrhythmia Note that the individual waves of the electrocardiogram bear the same relationship to one another in all leads However the space between the T waves and the next P waves (T P interval) varies with each beat The remaining features of this record are normal

Very rarely the sinus node may fail to generate an impulse for contraction (see Fig 180 A) The result is a dead string and one beat of the heart is entirely blotted out The pause here is usually equal to two cardiac cycles Administration of atropine blocks the terminal branches of the vagus and tends to abolish the arrhythmia Figure 180 A is the tracing of a healthy young athlete who came to the hospital for study because the school physician detected dropped beats on auscultation Sinus arrest

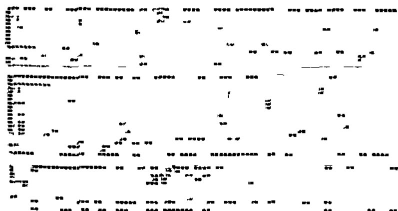


Fig 194 Sinus arrhythmia A slowing occurs during expiration and a quickening during inspiration

or standstill of the entire heart for one or two beats is caused by either failure of the sinus node to initiate the contraction impulse or the block of this impulse before it reaches the auricular muscle Its presence may be suspected clinically when a dropped beat is noted by auscultation However its true character can be recognized only when an electrocardiographic examination is made Vagal arrhythmias of this type are not unusual in well trained athletes

In Fig 180 B the same condition is seen Here however, it accompanies a deeply inverted T wave in lead 1 This patient had cardiac enlargement of the hypertensive type and a history of two episodes of prolonged chest pain following coronary occlusions In this case the sinus arrest was undoubtedly caused by a deficiency of the blood supply to the myocardial area containing the pacemaker

Very rarely two beats may be omitted The tracing shown in Fig 180 C was taken the day after an attack of chest pain lasting an hour in a man of 50 who had a previous history of hypertension The patient was sent to the hospital as a case of posterior coronary occlusion inasmuch as the

sudden fall in the pulse rate closely following the attacks suggested complete heart block Since the blood supply to the bundle arises from the posterior coronary artery, an involvement at this site was suspected However only a very slight increase in the P R intervals was noted The sinus arrest disappeared in a few days and the patient made an uneventful recovery

In Fig 195 an interesting variation will be noted After the third auricular beat a block of the impulse for contraction occurs at the sinus node In this instance the long pause is not interrupted by the occurrence of a P wave A slightly abnormal ventricular complex first appears This shows an important cardiac protective mechanism When the impulse for contraction failed to arrive at the A V nodal tissues in a time far exceeding the usual diastolic pause, the A V nodal structures in the emergency assumed the role of pacemaker and generated the impulse for contraction This phenomenon is known as VENTRICULAR ESCAPE Note the slightly different form of the ventricular complex in this cycle and the absence before it of the P wave of auricular contraction Both auricles and



FIG 195 Ventricular escape See text for explanation

ventricles in this instance contracted together Consequently the P wave is buried in the QRS The next impulse for contraction comes from the usual site in the sinus node as is shown by the reappearance of the normal P wave While ventricular escape is of no clinical importance it demonstrates the fine adjustment of the cardiac mechanism in the event of failure of the usual impulse for contraction It is likewise another example of the value of the electrocardiograph in explaining the cause of an abnormality of cardiac rhythm

Vagal action may also cause a shift in the pacemaker or site of impulse formation in the sinus node or it may cause the pacemaker to move down to the A V node for the space of a few beats A close study of Fig 196 reveals in addition to the bradycardia a variation in the duration of the P R intervals At times the P wave is buried in the QRS (first beat of lead 1) or it may be seen budding from the upright limb of the QRS (second beat in lead 2) Here the pacemaker is shifting or wandering back and forth between its usual site and the A V node THERE IS LITTLE OR NO CHANGE IN THE FORM OF THE QRS GROUPS WHEN THE IMPULSE FOR CONTRACTION ARISES ABOVE THE A V NODE Wandering pacemaker is again one of the finer points in electrocardiographic diagnosis and usually has no clinical significance

When the site of origin of the impulse shifts to the nodal tissues and

remains there A V nodal rhythm is said to be present Figure 197 shows this mechanism Note the absence of P waves the regular rhythm and the slow ventricular rate [4] The P waves are buried in the QRS groups This

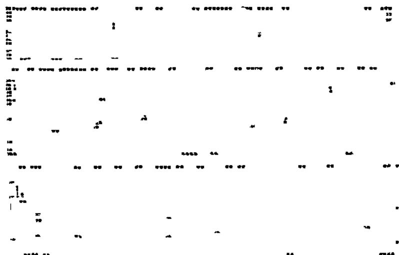


Fig 196 Wandering pacemaker Note the variations in the P R intervals in all leads as the site of impulse formation shifts from the sinus node to sections of the A V node

rhythm was recorded during the course of digitalization of a patient of 75 years of age who was suffering from arteriosclerotic heart disease and congestive failure In this instance it was a very important electrocardio-

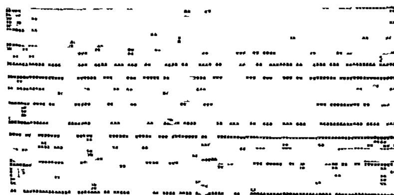


Fig 197 A V Nodal Rhythm Impulse a e from the A V node consequently auricle and ventr cle contract together and the I wave s bur ed in the QRS Rate 45

graphic finding The Heart Station called the ward to stop the digitalis since nodal rhythm often appears as a sign of beginning toxic action of this drug (page 8)

## PREMATURE CONTRACTIONS

### (Extrasystoles)

The ability to generate impulses for contraction is not a property possessed by the conduction system alone Any part of the heart structure may independently initiate these impulses and the electrocardiogram will show the presence of an isolated beat unrelated to the existing rhythm Since these beats arise from an abnormal focus they are spoken of as ectopic They arise before the next beat is due and consequently are also referred to as premature (The older textbooks called them "extrasystoles") These premature beats generally possess characteristic features that permit us

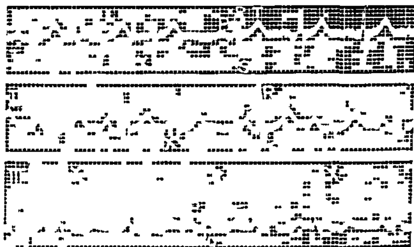


FIG 198 Premature auricular contractions In leads 2 and 3 the regular rhythm is interrupted at the sites marked x by premature beats from an abnormal auricular focus The P waves are smaller and the P R Intervals are shorter The site of origin of the beats is therefore low down in the auricle near the A V node

to place the abnormal focus for impulse formation in the auricle the A V node the bundle of His or the ventricles

If the premature contraction interrupts regular cardiac rhythm it is usually followed by a long pause known as the compensatory pause The first impulse arising from the sinus node following the premature beat is unable to initiate a contraction because of the refractory state of the heart muscle Consequently the whole heart pauses until the next impulse arrives from the S A node The unusually vigorous contraction that occurs after the premature beat is often felt and interpreted by the patient as "skipping" "a turn-over" or a "pounding" of the heart

Occasionally a premature beat may occur between two normal beats and not interrupt the dominant rhythm These are rare and are known as interpolated beats (see Fig 201 A) They are the only true extrasystoles

In the electrocardiogram the shapes of the premature beats arising in the same lead from identical foci are similar In the same lead differences in shape of two premature contractions from the ventricle point to two different foci

## Premature Auricular Contractions

Auricular premature contractions occur before the normal beat is due and are characterized by alteration in the P waves If the impulse arises in an auricular area outside the S A node the P wave shows a difference

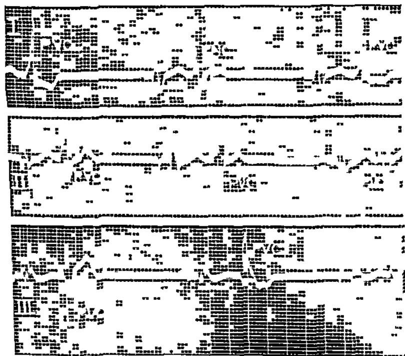


Fig 199 Nodal and ventricular premature contractions The premature beats are marked

in its shape In lead 2 of Fig 198 the third beat has a P wave of different shape since its point of origin is low down in the auricular musculature near the A V node Inasmuch as the distance to the nodal tissue is now shorter the P R interval is decreased In G of Fig 179 two premature beats of auricular origin are seen to occur together Their abnormal site of origin is indicated by the inversion of the P wave in each instance The QRS complexes of the auricular premature beats are similar to the others in the lead since the impulse descends to the ventricles along the normal conduction pathways Occasionally however the

ventricular beat may be slightly different in contour when the period of rest has been insufficient In some instances auricular premature beats may bring to light an early conduction defect For example the P R interval following a premature beat may be unduly prolonged and exceed the P R interval of the normal beats in this case we assume that some pathologic process is responsible for the tissue changes contributing to this delayed conduction

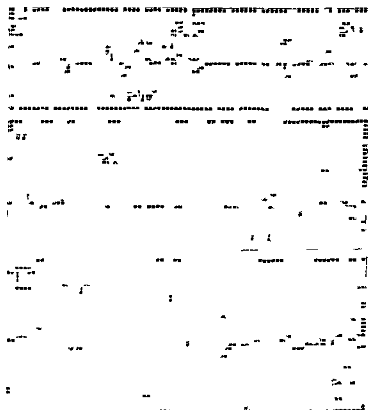


Fig 00 Premature ventricular contractions from foci in both ventricles

If the focus for the premature beat is in the A V node the auricles and ventricles often contract together because of the spread of the impulse in both directions (Fig 199, lead 1 beat 3) In this event the P wave may be buried in the QRS although in some instances it may follow the ventricular complex Occasionally the impulse reaches the auricle first and the auricular contraction precedes the ventricular In this instance however the P R interval will be much shorter than that observed in normal beats If the site of origin of the premature beat is very low in the A V nodal tissue the configuration of the QRS groups that follow may be slightly aberrant (Fig 199 lead 2 beat 2 See also Fig 195 beat 3)

Where auricular contraction follows an impulse traveling in a reverse direction along the specialized tissues we speak of this phenomenon as retrograde conduction

## Premature Ventricular Contractions

Premature ventricular contractions occur most frequently and are the usual cause of skipped beats They are readily recognized in the electrocardiogram (Figs 199 200 201) An impulse arising in the muscle of either ventricle causes premature contraction of both ventricles but the chambers do not contract together since it takes longer for the impulse to traverse nonspecialized muscular tissue For this reason the ventricu-

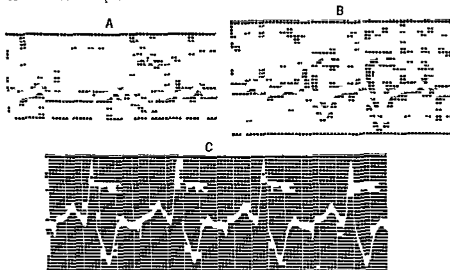



Fig 201 Premature ventricular contractions A single or isolated B in pair The same irritable focus sends in two impulses for contraction C premature beat following each normal beat

lar complexes of the premature beats are wider than normal beats The irregular spread of the impulse often causes notching and the complexes are not preceded by P waves The rhythmic production of stimuli by the S A node is unaffected After the ventricles respond to the premature beat they are in a refractory state when the next impulse arrives from the pacemaker Consequently there is a pause until the succeeding impulse reestablishes normal rhythm

Definite localization at the present time is not possible Ventricular premature beats may occur as single beats (Fig 201 A) less often they appear in pairs (Fig 201 B) Occasionally they may follow each normal beat (Fig 201 C) particularly when they appear as a manifestation of the toxic action of digitalis It is usually stated that showers of premature beats from a variety of foci in auricles or ventricles or both are more apt

to occur in the presence of cardiac damage However, I have seen many exceptions to this rule

## THE PAROXYSMAL TACHYCARDIAS

Premature beats from any site may occur in short runs because of the fact that the ectopic focus takes complete command of the cardiac rhythm

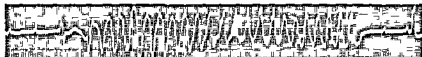


FIG 202 A short paroxysm of ventricular tachycardia The onset and offset are seen Similar paroxysms in this patient terminated in paroxysms of ventricular fibrillation For this reason this irregularity is referred to as the prefibrillary type of ventricular tachycardia

and sends in a succession of stimuli (Fig 202) We may refer to this event as either a series of premature ventricular contractions or a short *run of tachycardia If the focus is in the auricle, we speak of the condi*tion as paroxysmal auricular tachycardia (Fig 203) Similar paroxysms may have their origin in an A V nodal focus (A V nodal paroxysmal tachycardia) (Fig 204)

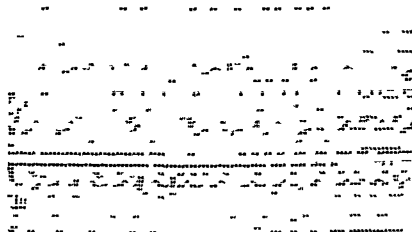


FIG 203 Paroxysmal auricular tachycardia

Clinically these paroxysms are characterized by the abruptness of their onset and offset and occur in patients who have no other sign of a cardiac abnormality as well as in those who present definite evidence of heart disease In most instances it is remarkable how well the heart muscle s ands the strain of these abnormal seizures The complete absence of any of the usual signs of failure speaks well for the functional integrity of the myocardium in such cases Of course in older people who have degenerative changes the

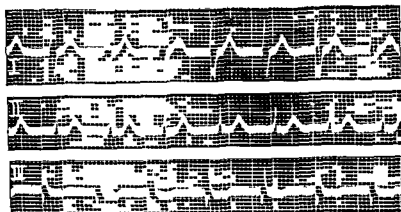
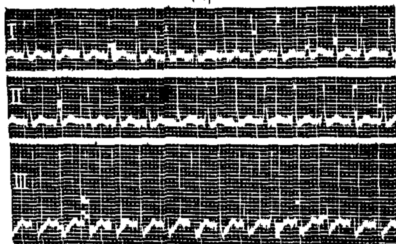



Fig 04 Paroxysmal nodal tachycardia

(A)




B




Fig 05 A Three leads of a tracing taken during a paroxysm of auricular tachycardia
B Paroxysm abolished by pressure over the right carotid sinus (applied at x)

sudden onset of a paroxysm of tachycardia may be followed quickly by evidences of cardiac failure or acute pulmonary edema The situation is then a medical emergency

In Fig 205 A we see three leads of a paroxysm of auricular tachycardia In B of this figure a tracing of lead 2 was taken while pressure was made over the right carotid sinus There is prompt return of sinus rhythm at the point marked 'X' Figure 206 shows a similar paroxysm in another patient, also stopped by carotid sinus pressure

Paroxysmal ventricular tachycardia (Fig 207) is a much more serious irregularity and occurs in the presence of organic heart disease The rate



FIG 206 Three leads of an electrocardiogram showing the onset and offset of a paroxysm of auricular tachycardia The onset followed the second beat in lead 3 Note the inversion of the P wave in this lead indicating abnormal auricular focus The paroxysm was terminated at point marked 'x' by carotid sinus pressure

is usually slower than that of auricular or nodal tachycardias and varies from 130 to 170 beats per minute The tracing has the appearance of a series of premature ventricular contractions This is not unusual since a paroxysm of ventricular tachycardia arises from an ectopic focus in the ventricular muscle The QRS groups in these paroxysms are widened and usually notched

Paroxysmal ventricular tachycardia is often irregular while the other varieties are perfectly regular The two main causes of paroxysmal ventricular tachycardia are myocardial infarction and the administration of excessive doses of digitalis to a patient who has a badly damaged myocardium

The prefibrillary type of ventricular tachycardia is a dangerous as well as an imperfectly understood mechanism (see Fig 214 A) It is dangerous

because of the frequency with which it terminates in ventricular fibrillation Some observers believe that this arrhythmia is caused by a circus movement in the ventricle similar to the circus movement described by Lewis as occurring in the auricles They refer to it therefore as ventricular flutter

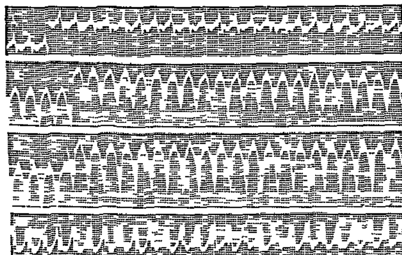


FIG 07 Ventricular paroxysmal tachycardia The onset follow d an attack of acute coronary occlusion It was abolished by quin d ne

In ventricular fibrillation the appearance of the tracing is characteristic (Fig 208) The waves show a disorderly arrangement and vary in size shape and duration from cycle to cycle There are only about 17 instances in the literature of recovery from ventricular fibrillation that are supported by electrocardiographic evidence Ventricular fibrillation no doubt



FIG 08 Ventr cular fibrillation Note irregular coa se type of curve that var es from beat to beat This tracing was obtained during an Adams Stokes se zure in a patient suffer ng from hypertens ve card vascular disease compl cated by complete heart block

occurs more often than it is recorded I have seen two cases both of which were associated with varying degrees of A V heart block (see Chapter 12)

## HEART BLOCK

The pathway followed by the excitation wave from the auricle to the ventricular muscle has already been described Disease processes affecting

the bundle of His may delay the passage of this impulse, or if more extensive, may block it altogether The function of conduction in the bundle may likewise be depressed by an overactive vagus but rarely to the stage of complete heart block When myocardial invasion takes place particu

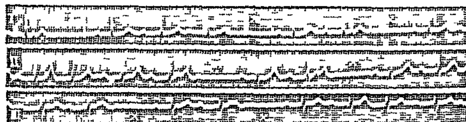


Fig 209 Incomplete heart block Dropped beats occur at sites marked "x" Note gradual increase in conduction time until beat is dropped (Wenckebach phenomenon)

larly of the diphtheritic type, the first hint of mischief may be indicated by a prolongation of the P R interval beyond the normal limit of 0 20 second (see Fig 181) If the lesion progresses the bundle may show an increasing inability to conduct impulses In this event the P R intervals gradually lengthen until a stage is reached where there is a total failure of the

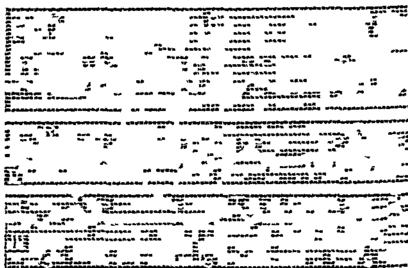


Fig 10 Heart block In this record every second beat is dropped

impulse to traverse the bundle (Fig 209) A beat will then be dropped out With this short rest, the bundle may be able to conduct the next impulse and a shorter P R interval appears The same process is then repeated until another beat is dropped This gradual increase in the duration of the P-R interval that ends in the total failure of the bundle to conduct

an impulse is known as the Wenckebach phenomenon The dropped beat is characterized clinically by an interruption of the pulse at the wrist and precordial silence The latter distinguishes between the pause of heart block and the pause following premature beats The extra sound produced by the premature beat may be readily ausculted The first stage of heart block eludes detection however and the electrocardiogram must be depended upon to make the diagnosis

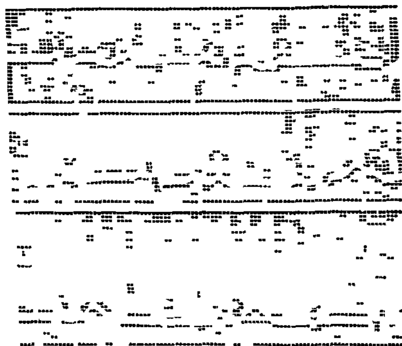


FIG 11 Complete h art block Auricula rate 76 Ventricular rate 38 The s nus node continues to control aur cular activity but the ventricles beat in response to a p cemaker that in tiates impulses for contract on at a slov er rate below the site of the les on

With progress in the lesion the blocked impulses may occur after each second beat (Fig 210) This is known as two to one heart block The ventricular rate is exactly half the auricular rate Complete dissociation or complete heart block between auricles and ventricles next occurs (Fig 211) and in order to survive the ventricles must establish a new center for impulse production below the level of the lesion This is exactly what happens the new center generally forming in the auriculoventricular tissues above the branching of the bundle The ventricular beats that are produced by stimuli from this site at a rate of 30 to 40 per minute show slight differences when compared to normal beats Often the disease process may extend down the conduction system to a lower level and the new

center may arise in one of the bundle branches The ventricular complexes are then widened and resemble those obtained in block of the bundle branch

Patients with heart block may be subject to Adams Stokes attacks at the time when complete heart block occurs The electrocardiograph in recent years has shed considerable light on the mechanism of cardiac action during and following these seizures Our laboratory has succeeded in taking tracings of three patients during Adams Stokes seizures Two of

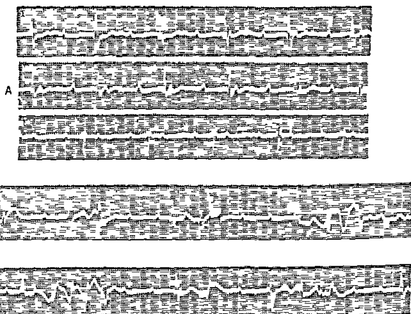



FIG 212 The electrocardiogram during Adams Stokes seizures For explanation see text

these patients developed attacks in the course of A-V heart block complicating hypertensive cardiovascular disease and the third following the onset of complete heart block that accompanied an acute (posterior) coronary occlusion The complete electrocardiographic records of cases 79 and 80 are included here with detailed interpretation

* FIG 212 A (Case 79) shows persisting complete heart block with auricular rate 88 and ventricular rate 44 The QRS complexes are notched and widened in all leads and left axis deviation is present Strips similar to B were observed to occur immediately prior to an onset of Adams Stokes seizure Here there are numerous premature beats occurring singly and at the end of the strip in pairs The auricular rate following the ectopic beats is more rapid than in the control averaging 107 beats per minute Strip C of Fig 212 is similar to B with the exception of the number of premature ventricular beats seen to occur in succession Short runs of three are present at the beginning and end of the strip

In Fig 213 Strips A B and the first half of C represent a continuous tracing taken during an *Adams Stokes seizure Strip A shows the prefibrillary type of ventricular tachy*

* This fine print can be omitted by the reader without destroying the continuity of the text

cardia with a rate of 210 per minute Some slight irregularities are present in thi strip but on the whole all of the widened complexes conform to the same pattern In strip B from X1 to X there i a change in the configuration of the ventricular com plexes they become widened and differ in shape from beat to beat The last part near X is quite typical of ventricular fibrillation From the point X2 to the end of the strip B we again note the presence of th prefibrillary type of ventricular tachycardia This arrhythm a continues throughout the first part of strip C At the middle of C a strip of tracing showing an arrhythmia similar to A and C is omitted Thirty seconds later the second part of strip C was obtained th s sho s a typical attack of ventricular fibrillation Note the presence in this strip of auricular beats Strip D is continuous

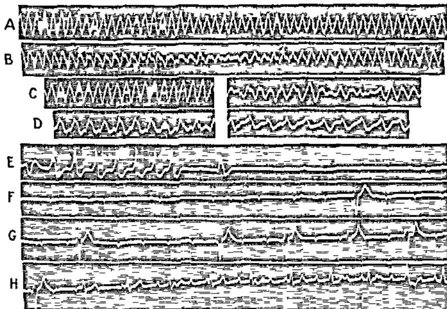



Fig 13 Electroc rdio am ecorded dur ng Adams-Stok s se zure See text for expla nat on

with C and sho vs emergence f om an attack of ventricular fibr llat on The QRS groups are widen d nd slurred and there appears to be a P wave b fore each QRS group Th w dth of the QRS complexes dec ases to ard the end of the str p The last half of trip D taken a minute later shov biza re configu at n of the QRS groups with S T interval depress on Ten attacks were reco d d showing electroca dio raphi find ngs sim lar to those d scr bed above

The next attack i sho n in strips E to H of Fig 13 this i a continuous record and is ncluded to sho v a d fferent type of emergence In strip E the QRS complexes are markedly aberrant with deep S T int rvals The rate of these complexes grad ally d creases toward the end of the str p The e is a slight pause toward the m ddl of the strip and this s followed by an ectop beat which init ate a per od of ventricular standstill lasting 16 8 se ond Au icular be ts are seen at fir t coming through at a very slow rate and then grad ally inc easing in frequency A ventr cul ectop c beat is s en toward the end of the str p th s niti tes a return of th v nt cular beats whi h occ r first at cycle length of 4 6 and then 4 2 and 2 0 seconds The rate of the ventr cular beats gradually increases until at the beg nn ng of str p H the rate ap

proaches 50 per minute The auricular rate in this strip is also rapid averaging 125 per minute Looking back on the auricular beats in strips F and F they will be seen to vary in shape This is probably because of the fact that the beats arise from different foci in the auricular muscle

Fig 214 shows additional interesting features of some of the shorter paroxysms that were recorded Strips A and B are continuous At the start of strip A there are five successive ventricular premature beats followed by a pause The next ventricular premature beat initiates a short paroxysm of the prefibrillary type of ventricular tachycardia The shape and the amplitude of the ventricular complexes of this paroxysm show a gradual change The last cycles are quite aberrant Strip B shows complete A V heart

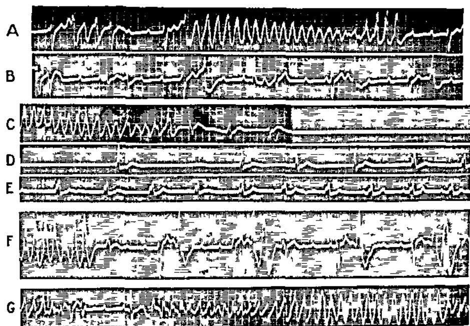



FIG 14 Tracings recorded during shorter seizures in same patient See text for explanation

block interrupted by numerous premature beats from various foci C D and E are continuous strips In the first part of C we note a paroxysm of prefibrillary type of ventricular tachycardia This ends with the appearance of an idioventricular rhythm the rate of which is 52 per minute The idioventricular center however apparently fails for a period of 8 2 seconds during which time complete cardiac standstill is observed The auricular beats are likewise absent in this strip The function of the idioventricular center gradually returns and occasional cycles are seen in strip D These recur with greater frequency until a rate of 46 per minute is reached in strip E The ventricular complexes however are considerably widened measuring 0 16 second There is complete absence of auricular beats from point Y in strip C to point Z in strip D In the beginning of strip E the auricular rate is slow measuring 40 per minute this gradually increases in frequency until at the end of strip E it approaches the rate of 100 per minute Strips F and G are a continuous tracing At the beginning of strip F there is a short paroxysm of the prefibrillary type of ventricular tachycardia terminating in a single ventricular ectopic beat Following this the idioventricular center continues to be interrupted by the occurrence of numerous ventricular premature

beats some in couples and others appearing in pairs Strip G shows several paroxysms of the prefibrillary ventricular tachycardia with ventricular complexes of different types

Fig 215 A shows a three lead control tracing of the type obtained on the patient whose history appears in Case 80 A two to one A V heart block with auricular rate of 80 and ventricular rate of 40 is present Note the *widening and notching of the* QRS complexes in leads 2 and 3 In strip B sinus rhythm is seen with prolongation

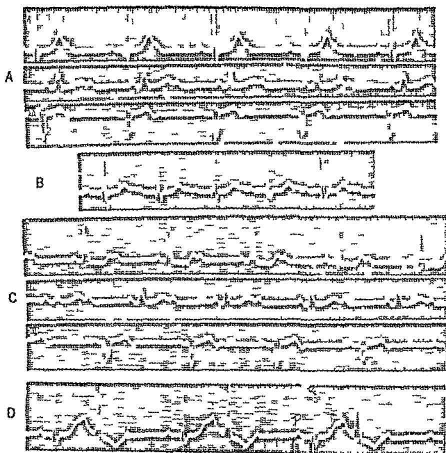


Fig 215 Control tracings (Case 80) taken before onset of Adams Stokes seizures For explanation see text

of the P R intervals to 0 3 second Strip C shows a two to one heart block with QRS complexes notched and widened in all leads Note the difference between QRS1 of this strip and QRS1 of strip A Strip D shows a two to one heart block with coupled ventricular premature beats from various foci This tracing preceded the paroxysm of prefibrillary type of ventricular tachycardia

In Fig 216 A to F is a continuous tracing obtained during a typical Adams Stokes seizure Strip A shows a prefibrillary type of ventricular tachycardia with ventricular rate of 300 per minute These complexes present a definite regularity in rate as well as in form although in different places in the lead a slight difference in

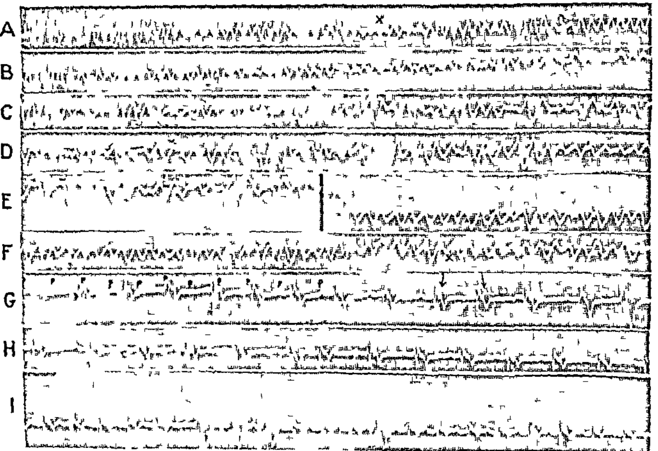



FIG 16 Long paroxysm of prefibrillary type of ventricular tachy and a terminating in ventricular fibrillation with recovery For detailed explanation see text

shape is noted For instance at point X sufficient irregularity exists to constitute a short paroxysm of ventricular fibrillation The first third of strip B is the same as A in th la t two third of this strip the ventricular complexes are s en to become more irregular than in th previous strip From the end of strip B and in luding strips C D E and F v e see a continuous paroxysm of ventricular fibrillation Note the extreme irregularity in the siz amplitude and sequence of the ventr cular complexes In some places a semblance of regularity may be noted but this is present for an extremely brief period The total duration of thi paroxysm of ventricular fibrillation is 4 seconds Auricular beats can be noted in places during the above paroxysm Figure 16 (G to I) was made a fe v seconds after the end of the paroxysm and shows complete A V d ssoc ation v ith auricular rate of 140 and a ventricular rate of 64 Note th R T elevation in the initial cycles gradually decreasing to vard the end of the str p v here the R T segments are practically at the isoelectric line Here the auricular rate and the id oventricular rhythm are much more rapid than in th control tracing This is not infrequently observed immediately following emergence from a paroxysm th anox c state actin as a st mulant to the respective centers Note that the la t cycle of strip G is aberrant Strip H shows that the grade of heart block is nov ti o to one ind cating a return to more normal function across the A V nodal tis ues This is maintained to th end of the strip with a gradual increase in the rate of the idioventr cular center Strip I shows a prolongation of the P R intervals to 0 3 second ith a one to one respon e Occasional ectopic beats are seen

The Adams-Stokes seizure recorded here was the only one that the patient had during her two v eeks stay n the hospital She was ambulatory on di charge A follow up letter at the end of five m nth found her in fairly good condition She reported no recurrence of the seizures

## BUNDLE BRANCH BLOCK

Various pathologic processes may cause block of the bundle on either side The appearance of the electrocardiogram obtained under these cir

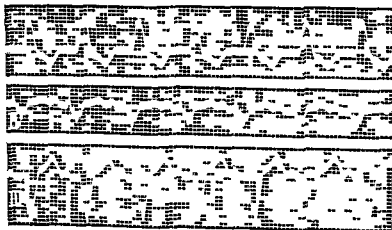


FIG 17 Bundle branch block Note the wid ned notched QRS complexes with the T v ave oppo ite n direction to the main complex This is common type of tra ing It results from block of the left bundle branch

cumstances may be understood if we follow the happenings in the heart The ventricle on the side of the intact bundle branch contracts first The

impulse then travels through nonspecialized muscle tissue to the opposite ventricle where a delayed contraction occurs This is reflected in the appearance of the electrocardiogram The QRS group is widened because of the longer time consumed by the impulse in spreading through nonspecialized tissue of the muscle and notched because of the irregularity of this spread The T waves are usually opposite in direction to the main deflection of the QRS Increased voltage of the QRS is usually present To determine the site of the lesion apply the same rule as in axis devia-

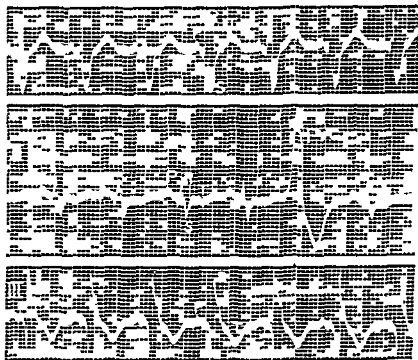


Fig 218 Right bundle branch block An isolated premature ventricular contraction is seen in lead 2 This is uncommon type of bundle branch block

tion * For example in Fig 217 the QRS groups are upward in lead 1 and downward in lead 3 This is complete block of the left bundle branch (common type) In Fig 218 the QRS groups are down in lead 1 and up in lead 3 This is complete block of the right bundle branch At times we see the QRS groups widened and directed upward in all three leads Although previously referred to as arborization block or block in the Purkinje network these tracings are now regarded as partial block of the main bundle branches (Fig 219) In some cases of this type the bundle branch block may not be complete and a return to normal conduction may be seen every third or fourth beat (Fig 220)

* This is still a controversial question Some authors do not agree with the views *presented here*

When bundle branch block is seen we can usually be safe in suspecting myocardial damage There are however some exceptions to this rule When a bundle branch block is associated with a short P R interval (Fig 221) it should not be viewed as a sign of disease These patients

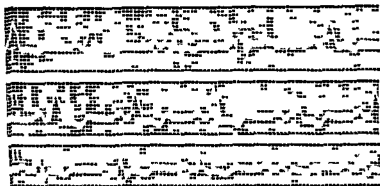


Fig ?19 Intraventricular block

are often subject to attacks of paroxysmal rapid heart action To explain the occurrence of functional heart block of the bundle branch type it has been claimed that an additional conduction pathway (bundle of Kent)

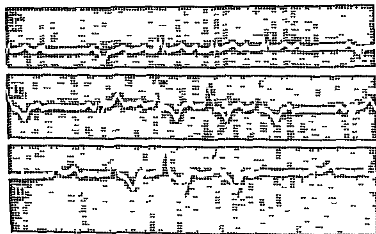


Fig 0 Transient bundle branch block

is present that transmits the impulse in a shorter time than it takes to traverse the usual pathway In some cases a series of sudden attacks of paroxysmal tachycardia arising from an auricular focus may severely tax the conduction system Notching of the QRS may be present and in some cases a widening of the QRS may be seen in normal individuals Here

again is an instance where the electrocardiogram must be interpreted entirely in the light of the clinical findings

A diagrammatic summary of the more common types of tracings associated with block at various levels in the conduction system is shown in Fig 222



Fig 221 Bundle branch block with short P R Intervals

## AURICULAR FLUTTER

The term auricular flutter has been advanced for an uncommon but interesting derangement of auricular function characterized by the establishment of an abnormal circulating contraction or flutter wave Flutter is supposedly produced by the continual passage of this wave around the auricular musculature near the entrance of the great veins (circus movement) Each time the wave passes, there is a radial spreading of the contraction impulse (Fig 223) When the electrocardiogram records this movement of the flutter wave, in a favorable lead the string will be seen to be in continual motion The auricular rates in cases of flutter are high averaging from 250 to 360 per minute Fortunately the ventricle even if healthy, could not respond to all the impulses arriving at the A V node Usually every second impulse penetrates and causes a ventricular contraction i e a two to one heart block is present Varying grades of block may appear consequently the pulse at the wrist in auricular flutter may be 120 to 170 When the slower ventricular rates are present the condition is often missed because it is unsuspected In flutter the heart rate is constant in all positions Pressure over the carotid sinus however, may be used to distinguish between paroxysmal tachycardia and flutter If flutter

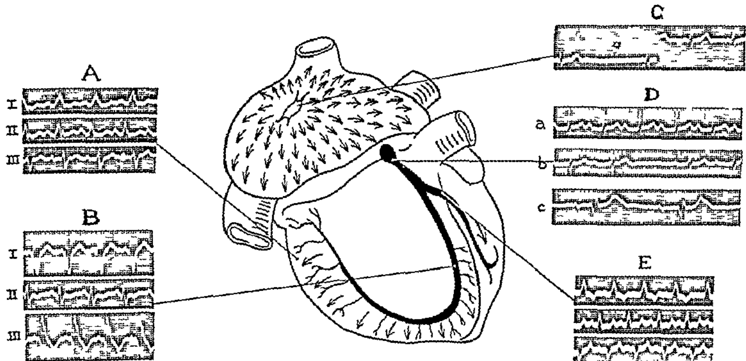



Fig 27 Diagram illustrating various types of block and the site of the lesion in the conduction system in each instance A Intraventricular (arborization) block B Right bundle branch block C Sinus arrest (sino auricular block) D Heart block a Prolongation of P R Interval (first stage) b Dropped beats c Complete dissociation E Left bundle branch block

is present carotid sinus pressure may cause a sudden halving of the pulse rate If this does not take place the pulse in flutter will usually become

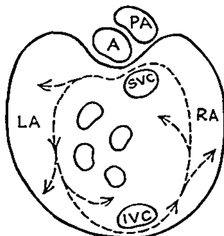



Fig 223 Diagram showing course of flutter wave in the auricle (Redrawn from Pardee) *

slower and often irregular Carotid sinus pressure in cases of flutter may even cause ventricular stand still while in paroxysmal tachycardia if the

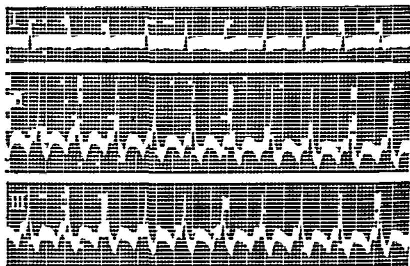


Fig 224 Auricular flutter The ventricle contracts following each second revolution of the circus wave (2 1 response)

attack is not stopped and normal rhythm restored no effect whatsoever will be noted on the rate or rhythm of the pulse If the patient is in re

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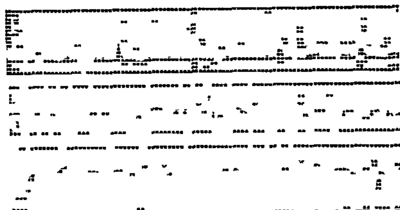


Fig 25 Auricular flutter There is a ventricular response to every third flutter wave (3 1 response)

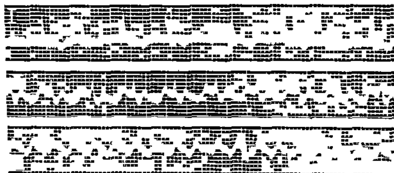


Fig 26 Auricular flutter In lead I note the varying degrees of ventricular response

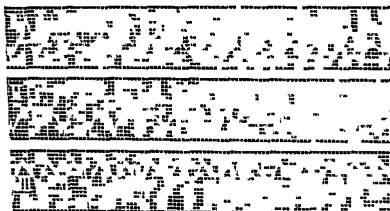


Fig 27 Auricular flutter 1 to 1 ventricular response

cumbency in the proper light the neck veins may be distinctly visible in which event the very rapid flutter movements are often observed as they are transmitted back along the venous column from the auricle In many

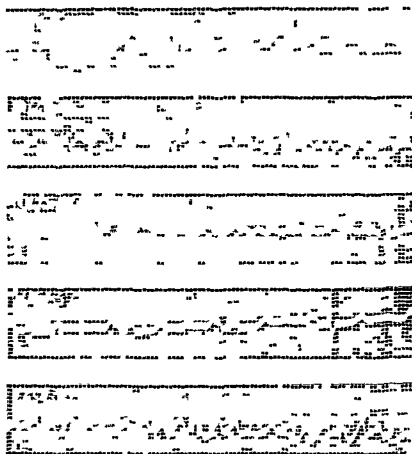


FIG 28 Series of electrocardiograms (lead 2) illustrating the effect of digitalis on auricular flutter A Normal rhythm B Auricular flutter Varying degrees of ventricular response C Following administration of digitalis The flutter has been converted into fibrillation D After withdrawal of digitalis normal rhythm appears E Recurrence of flutter two months later This patient had rheumatic heart disease cardiac enlargement and advanced mitral stenosis

cases although flutter may be suspected it cannot be diagnosed without an electrocardiogram

The appearance of the tracing in auricular flutter is characteristic (Fig 224) The flutter waves are generally seen to the best advantage in leads 2 and 3 where they appear as uniform up and down oscillations Closer inspection shows that the auricles as a whole appear to enjoy no period

of diastole for there is seen no beginning and no ending of the auricular movement The ventricular rate in flutter depends on the degree of A V block While a two-to-one block is usually present higher and even varying degrees of block are not uncommon (Figs 225, 226 228) A few cases where the ventricle has responded to every wave of the circus movement (one to-one response) are on record These are serious happenings particularly in diseased hearts since the strain on the myocardium is usually proportional to the increase in the ventricular rate The patient whose tracing appears in Fig 227 was a housewife of 52 who suffered from coronary disease and hypertension She died suddenly a few minutes after the onset of an attack of auricular flutter with a one to-one response This fatal attack was similar to the one recorded here

Digitalis is the drug of choice in flutter and should be given in full dosage to increase the grade of A V block Following digitalis a two-to-one response may be converted into a four to one The action of this drug may be watched by a series of electrocardiograms If the digitalis is continued fibrillation replaces the flutter and when the drug is withdrawn sinus rhythm usually returns (Fig 228) Although quinidine has been recommended digitalis is generally more successful in bringing relief to the patient with this type of circus movement and is the drug of choice Flutter commonly complicates thyrotoxic and rheumatic heart disease and may appear suddenly in patients suffering from arteriosclerotic heart disease It may occasionally appear in patients of any age who have apparently normal hearts (paroxysmal flutter) (page 391)

## AURICULAR FIBRILLATION

Auricular fibrillation is closely allied to auricular flutter and is by far the most important of the cardiac arrhythmias Here again it may be useful to recall the circus movement theory of Garrey in order to obtain a clear understanding of this mechanism In flutter the circus movement takes the same pathway through the auricular muscle at each revolution In fibrillation the course of the circus is wholly erratic (Fig 229) It weaves its way in and out of the auricular myocardium in an irregular fashion taking the course permitted by the physiologic state of the muscle at the moment Co-ordinated auricular contractions cease The circuits of fibrillation are completed at varying times but are al

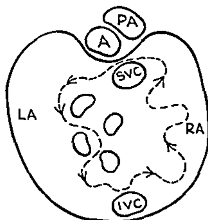



FIG 229 Diagram showing irregular course followed by the fibrillation waves in the auricular muscle

ways more rapid than in flutter Auricular fibrillary rates of 400 to 600 are not uncommon In consequence the ventricular response to the series of rapid irregular impulses arriving at the A V node is likewise irregular A typical electrocardiogram of fibrillation is shown in Fig 230 Note first the absence of the usual P waves that represent co-ordinated auricular con traction At times in place of the auricular waves a series of irregular 'f or fibrillation waves appear The QRS groups in auricular fibrillation are irregularly spaced and are of supraventricular type i e the origin of the beat is above the junctional or A V tissues

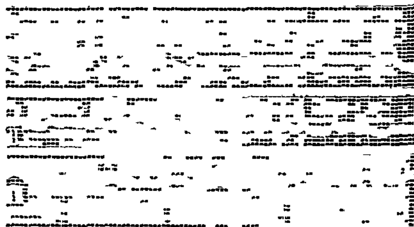


Fig 30 Auricular fibrillation Note total irregularity of the rhythm The P waves are replaced by f waves (seen best in lead 3 of this tracing) Note the depression of the S T intervals in leads 1 and caused by digitalis Left axis deviation is also present

The diagnosis of auricular fibrillation can nearly always be made clinically However if the ventricular rate is slow it may elude detection If it is possible to exercise the patient the distinction may be made at once since exercise increases the pulse irregularity in fibrillation At times premature beats occur with such frequency that the cardiac rhythm is entirely irregular Exercise abolishes the premature beats, and the rhythm of the heart becomes regular Premature beats may occur with auricular fibrillation but they arise always from a nodal or ventricular focus and never from a focus in the midst of such auricular turmoil

Auricular fibrillation may be permanent or paroxysmal The former is more common In rare cases the paroxysmal variety may be present and represent the only abnormality in the cardiac examination (page 595)

The f' or fibrillation waves may be quite prominent (Fig 230) espe cially when the arrhythmia complicates mitral stenosis and hypertrophy of the auricular muscle is present On the other hand in hearts with poor auricular myocardium, the 'f waves may be small or scarcely visible at all (Fig 231) In some leads the f waves may be so regular that they

suggest the presence of auricular flutter (Fig 228 C) The term impure flutter has been employed by some laboratories to designate this type of electrocardiogram and may be retained if preferred for these tracings probably represent a transition stage between flutter and fibrillation

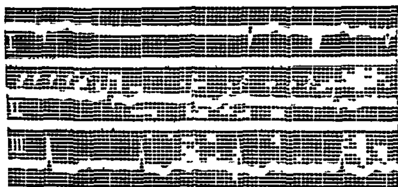


FIG 31 Auricular fibrillation Note absence of P waves th total irregularity of rhythm The S-T Intervals are depressed in leads 2 and 3 Right axis deviation is present

## CORONARY ARTERY DISEASE INCLUDING ACUTE MYOCARDIAL INFARCTION

Myocardial infarction that follows the occlusion of a coronary vessel produces characteristic alterations in the form of the electrocardiogram A study of these changes often enables the physician to state the site of the infarct while frequently repeated tracings or serial electrocardiograms are helpful in following the healing process

In recent years the contributions to this branch of electrocardiography have been many However a uniformity of opinion on all issues unfortunately does not prevail at this writing The terminology is likewise in an unsettled state While the recent standardization of the direct or precordial leads will ultimately be of great value at present much confusion exists regarding the interpretation of the tracings taken by the various technics In this brief sketch of electrocardiography I will try to avoid as much as possible the controversial points and briefly state the facts that appear at this time to be definitely established

At the start we must realize that the coronary arteries cannot influence the form of the electrocardiogram unless the blood flow through them is temporarily or permanently interrupted and the cardiac muscle is affected If serious disease of the walls of the coronary arteries is present but so situated that it does not interfere with the nourishment of the heart muscle no alterations appear For this reason an electrocardiographic diagnosis of uncomplicated coronary sclerosis is impossible However if a coronary artery is suddenly occluded with the production of an area of myocardial infarction marked changes usually appear sooner or later in the electro-

cardiogram in well over 90 per cent of the cases These changes first described by Pardee in 1920, take place in the RS T segment of one or more leads They consist of a downward, sharply peaked T wave (coronary T wave of Pardee) with an upward convexity of the RS T interval (Fig 232) *Following an acute infarction the RS T segment arises above the iso electric level (monophasic curve)* As healing progresses, the RS-T interval returns to the base line

The tracings obtained in the presence of an area of acute infarction usually fall into two groups Barnes and Whitten (1929) first designated

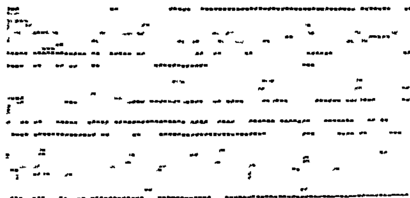


Fig 232 Electrocardiogram made 12 hours after an attack of severe chest pain in a man of 50 suffering from hypertensive cardiovascular disease Note the typical RS T interval elevation in lead 1 and the depression of the same segment in lead 3

these as the $T_1$ and $T_3$ types The $T_1$ pattern is characteristic of an infarction involving the anterior portion of the left ventricle and consists of an elevation of the RS-T segment in lead 1 and a depression of the RS T segment in lead 3 (Fig 232) Infarction of the posterior basal portion of the left ventricle produces an elevation of the RS T segment in lead 3 and a depression of the same interval in lead 1 (Fig 233)

Later investigations by Wilson (1933) first called attention to the importance of the initial deflection or Q wave in the diagnosis and localization of areas of infarction This investigator referred to the $Q_1$ and $Q_3$ types In the $Q_1$ type associated with an anterior infarction the Q wave appears and persists in lead 1 (Fig 234) while a posterior infarction may produce a deep Q wave in lead 3 (see Fig 237) It may be demonstrated by animal experimentation that curves of these types are routinely produced by an injury to the cardiac muscle of either the right or left ventricle [1]

Following an occlusion the area of injured muscle undergoes change from day to day This is reflected in the electrocardiogram but each patient will be found to differ in regard to the speed with which this variation takes place Characteristic alterations may appear in the RS T intervals 30 min

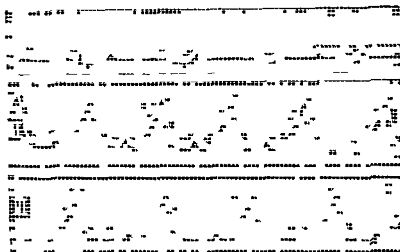


FIG 233 Tracing taken three hours after an attack of acute ind gestion in a laborer of 40 Both father and mother suffered from coronary disease with anginal seizures Note the RS T interval alterations in leads 2 and 3 The descending limb of the QRS group does not return to the base line but continues into a large T wave (monophasic curve)

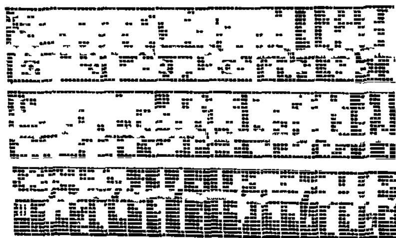


FIG 34 Evidence suggesti g an old anterior coronary occlusion Note th Q wave in lead 1 the flat T and diphasic T Invers on of T and left axis d viation are also present

utes after the seizure or they may be delayed for several days For this reason serial studies are advisable whenever the clinical features are suggestive and the initial electrocardiogram is negative

While the electrocardiogram in coronary occlusion may change its form from day to day the alterations are more marked and more rapid during the first weeks following the accident When healing of the infarct is complete the indirect (limb) leads may show a return to the normal configuration Frequently however the T-waves will remain inverted, and their peculiar cove like shape should at once arouse suspicion concerning their mode of origin (see Fig 238) The clinical history should then be searched for proof At times RS T deformities may return to normal with healing of the infarct but the reduction of the blood supply to a vital spot like the bundle of His may result in delayed conduction and a permanent prolongation of the P R interval However, when the only remaining feature of the occlusion is deeply inverted $T_3$ care should be used in its interpretation since inversion of $T_3$ is not an uncommon finding in normal electrocardiograms If a deep $Q_3$ is present we are more certain of the meaning of the deep $T_3$ but in the absence of the Q wave in lead 3 the clinical history is the only guide in the interpretation Lead 2 may help in making the decision 'M or W shaped complexes in lead 2 as well as a deep $Q_3$ should always make us suspicious of an old posterior infarction (see Fig 182D)

Alterations in the auricular complex have also been observed to follow an occlusion of the coronary artery Characteristic changes in the P waves and the P R segment have been produced in animals by compression of the auricular arteries and are directly related to the myocardial ischemia Similar changes have been observed in man following coronary occlusion There may be depression of the P R segment with notching and inversion of the P wave Arrhythmias may occur with the displacement of the pace maker from the S A node

Electrocardiograms following exercise are occasionally of value in clarifying the diagnosis of angina pectoris Where an objective method is desirable in insurance examinations or when the history is typical but the patient neurotic the appearance of characteristic changes in the RS T intervals or T-waves of the electrocardiogram following exercise may be valuable The normal patient will show no alteration in the T waves after exertion nor will he show depression of the RS T intervals exceeding 1 mm below the base line The patient with angina may show depression or elevation of the S T interval of over 1 mm in leads 1 and 2 following exercise often associated with some T wave inversion However a negative result does not exclude the diagnosis of angina

Similar alterations in the RS T segment and T wave of the electrocardiogram have been produced by Levy and his co workers in patients suffering from coronary sclerosis by inducing anoxemia A special apparatus is used for this test by means of which the patient breathes a constant percentage mixture of oxygen Levy reports alterations in the T wave in amplitude

and occasionally in direction and depression of the RS T segments in the indirect leads This test may also be of great value when the diagnosis is in doubt

## PRECORDIAL LEADS

Studies of the usual three leads by various groups of workers soon demonstrated that coronary occlusion in some instances could occur in the absence of the characteristic electrocardiographic alterations just described

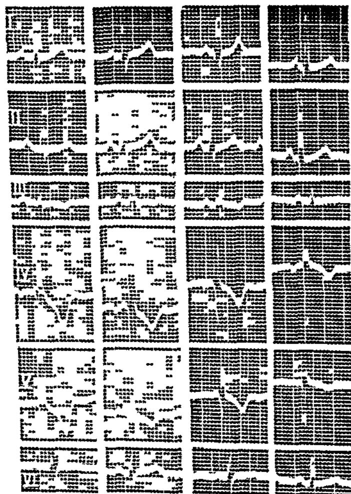


Fig 35 Seri s of normal six lead electrocardiograms taken by the old techn Lead 4—bet een apex beat and angl of left scapula; lead 5—between the apex beat and the l ft leg lea l 6—between the angl of the left scapula and the left leg Not th de p Q waves in leads 4 and 5 and inverted T waves in the same leads

Consequently the re introduction by Wood and Wolferth[4 0] in 1931 of Waller s method (1887) of applying electrodes directly to the chest wall was a valuable advance that greatly increased the efficiency of the electrocardiographic method in the diagnosis of cardiac infarction These investigators recommended a fourth lead obtained by applying the right arm electrode over the apex beat and the left leg electrode directly opposite

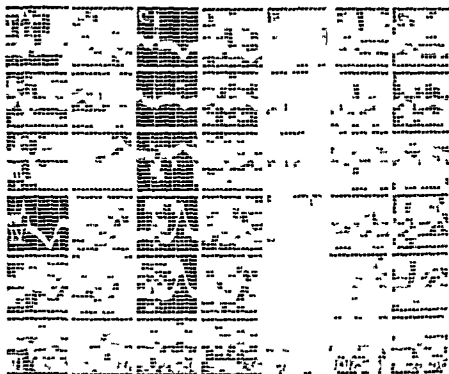


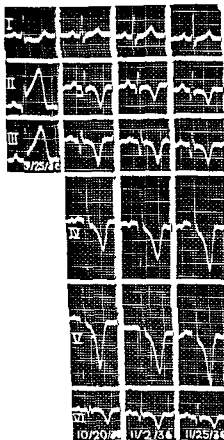
Fig 236 Serial tracings following attack of coronary occlusion (Case 40) The direct leads (4 5 and 6) were taken by the old technic In A the T waves in l ads 4 and 5 are inverted In B th y are upright Note the succession of changes in the T waves in lead 1 an l from A to C In G the indirect l ads are almost normal The alterations persist in the T waves of the direct leads

on the back of the chest at the level of the angle of the scapula In this original fourth lead (Fig 235) the first deflection was normally downward and was referred to as a Q wave the following upward deflection wa termed an R wave and the last deflection normally directed downward was called the T wave

Various studies of the fourth lead soon showed that in some cases it exhibited the characteristic features of occlusion when the usual three leads were normal In other instances it was found that it aided considerably in establishing more firmly the diagnosis suggested by the limb leads In

the presence of acute infarction in the anterior portion of the left ventricle significant changes occur in the fourth lead (Fig 236) The Q wave disappears The S T segment is depressed Gradually $T_4$ be comes upright and increases in height The T wave may later re turn to normal but the Q wave in this lead does not reappear When $Q_4$ is absent in the direct lead obtained by the use of the old tech nic this finding should always sug gest a previous anterior infarction even in the presence of normal in direct leads

A posterior infarction produces



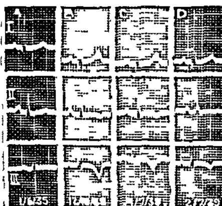




FIG 37 FIG 38

FIG 37 Serial trac ngs (old direct leads) following posterior coronary occlu ion Wh l T and T ar de ply nve ted the chan e in the usual or ind rect le ds a e char cter stic and fu n h sufficient ev d nc in this case

FIG 238 Ser al tracings (Ind rect leads) Pati nt an American voman of 55 who had no signs of cardiov scular disease on phys cal examination Th blood pres ure was 1 0/80 Ur ne n gativ Blood sugar normal A Electrocardiogram v as made b cause of pa n in th left elbow The pain was dull and unrelated to ex rtion Similar t acings were obtain d over the course of three years B Taken one ek after an attack of ind gestion The pa n wa ep gastric and lasted a few m nutes The findings suggest n area of nfarction on the posterior surface of the heart when co pa ed to A C and D show gradual disappearance of th signs from the record If D was obtained and other record of th s patient v ere not available a d agnos s of co onary occlusion could not be mad

changes in the fourth lead that are usually transient and much less marked The RS T segment is elevated and the depth of the T wave diminishes

The Q wave remains These changes fade rapidly and subsequent tracings show Q and T waves of increased amplitude In my experience the standard leads reflect the changes of a posterior infarction much more clearly than lead 4 (Fig 237) Consequently while the precordial lead is a valuable aid in the diagnosis of various types of myocardial injury study of the usual indirect leads should not be neglected (Fig 238)

When the use of the fourth lead became popular, many laboratories, as the result of continued experimentation with a number of connections from various locations on the thorax adopted their own combinations As a result no unanimity of opinion existed as to where the electrodes should be placed The confused situation that resulted discouraged the practitioner's attempts to learn at this time the features of many of the different combinations of chest leads A standard method of applying electrodes was very much needed to clarify the situation To this end in 1938 a joint committee appointed by the American Heart Association and the Cardiac Society of Great Britain and Ireland considered the matter and made the following recommendations with reference to the routine use of a single precordial lead *[3]

1 It is recommended that those who employ a single precordial lead place the precordial electrode upon the extreme outer border of the apex beat as determined by palpation If the apex beat cannot be located satisfactorily by palpation the electrode may be placed in the fifth intercostal space just outsid the left border of cardiac dulness, or just outside the left midclavicular line if percussion of the heart is unsatisfactory Where precordial leads are taken by a technical assistant the position of the precordial electrode should be marked on the chest by the physician

2 It is recommended that a single precordial lead in which the precordial electrode has the location specified in the preceding paragraph be known as *Lead IV B* when this electrode is paired with an electrode in the left interscapular region *Lead IV R* when it is paired with an electrode on the right arm *Lead IV L* when it is paired with an electrode on the left arm *Lead IV F* when it is paired with an electrode on the left leg and *Lead IV T* when it is paired with a central terminal connected through equal resistances of 5 000 or more ohms to electrod s on each of the three extremities mentioned

It is suggested that for all ordinary purposes *Lead IV R* or *Lead IV F* be employed The latter lead should have the preference until it has been established that the former which is somewhat more conven ent is equivalent to the latter for all practical purposes or yields results of equal value

3 It is recommended that in taking the precordial leads specified the galvanometer connections be made in such a way that relative positivity of the ap cal electrode is represented in the finished curve by an upward deflection (a deflection above the isopotential level) and relative negativity of the apical electrode by a downward deflection

It is urged that this convention be adhered to in case of precordial leads other than those specified and also in the case of all leads in wh ch the one electrode is placed much closer to the heart than the other In other ord it shall be the standard convention in taking such leads to make the galvanometer connections in such a way that relative positivity of the electrode nearer the heart is represented by an upward deflection

4 It is recommended that with the galvanometer connections made as described in

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the preceding paragraph the deflections of precordial leads be designated by the symbols P Q R S and T and that in the application of these symbols the same conventions be employed as in the case of the standard limb leads

5 It is recommended that in taking precordial lead the electrocardiograph be so adjusted that a deflection of one centimeter in the finished record corresponds to a potential difference of one millivolt as in the case of the standard limb leads Any reduction in sensitivity made necessary by very large deflections should be clearly indicated on the curve preferably by photographing the effect of introducing a potential difference of one millivolt into the galvanometer circuit

6 It is recommended that the greatest dimension of the apical electrode employed in taking the leads specified in this report be 3 cm or less A circular electrode between cm and 3 cm in diameter should ordinarily be employed (see Fig 174)

7 It is recommended that the terms Lead IV (R F etc) apical lead apex leg lead etc be used henceforth only in connection with the lead specified in this report

The standardization of the single precordial lead accomplished the American Heart Association has added a supplementary report for the workers who wish to employ multiple precordial leads A summary of the report follows

## Multiple Precordial Leads

When leads from two or more precordial points are employed it is suggested that the precordial electrode be paired either with an electrode on the left leg or with a central terminal connected through an equal resistance of 5000 or more ohms to electrodes on the right arm left arm and left leg It is suggested further that in the first case the letters CF followed by a subscript and in the second case the letter V followed by a subscript be employed to designate such leads

The position of the precordial electrode shall be indicated by the subscript used according to the following plan subscript 1 shall be used for the right margin of the sternum 2 for the left margin of the sternum 3 for a line midway between the left margin of the sternum and the left midclavicular line 4 for the left midclavicular line 5 for the anterior axillary line and 6 for the left midaxillary line When the letters and subscripts specified are employed it shall be understood that in the case of the sternal leads the precordial electrode has been placed in the fourth intercostal space and that in the case of the other leads it has been placed upon a line drawn from the left sternal margin in the fourth intercostal space to the outer border of the apex beat (or to a point at the junction of the midclavicular line and the fifth intercostal space) and continued around the left side of the chest at the level of the apex beat or of the junction mentioned

The advantages of making the galvanometer connections in such a way that relative positivity of the precordial electrode is represented in the finished curve by an upward deflection and relative negativity of this electrode by a downward deflection are as follows

1 This method makes it possible to assign the letters Q R and S to the individual deflections of the QRS group in exactly the same manner as in the case of the standard limb leads without violating the general principle that as far as possible deflections which have the same origin or the same significance should invariably bear the same name In particular it makes it possible always to assign the same letter (R) to the onset of the intrinsicoid deflection which signals the arrival of the impulse at the epicardial surface of the portion of the heart subjacent to the precordial electrode without departing from the customary method of labelling the QRS deflections

2 In cases of infarction of the anterior wall of the heart this method yields ventricular complexes characterized by abnormally large initial downward deflections (Q waves) and sharply inverted T wave of the cove plane of coronary type These complexes are practically identical with those which have long been considered

characteristic of myocardial infarction in the case of the standard leads and they may be d scribed in the sam terms

3 The P deflections and the T deflections are normally upright There are great advantages particularly from the standpoint of one who is teaching electrocardiography or of one who is beginning the study of this subject in a system which makes upright T waves invariably normal whatever the lead

4 The use *of the terms plus and minus and of the symbols + and — greatly sim* plifies things In the case of the precordial leads one electrode the precordial electrode is of much more importance than the other In the discussion of the principles upon which the interpretation of the precordial electrocardio gram rests it is necessary to refer frequently to the potential of the precordial electrode and in connection therewith to employ the terms and symbols mentioned *Since we are accustomed to* speak of downward deflections as negative and to prefix measurements of such deflections as negative much confusion and misunderstanding will be avoided if the deflection of the tracing is upward when the potential of the precordial electrode is positive and downward when the potential of the electrode is negative



FIG 239 Electrocardiograms of three normal persons including the direct lead (4F) recommended for routine use Note normal variations

**Nomenclature** For the convenience of those who wish to make statistical studies of the QRS group to measure and tabulate the QRS deflec *tions or to classify or characterize* QRS deflec tions of different types it is imperative that the individual deflections of the QRS group b designated by *distinct symbols even though the* naming of these deflections may involve the ap plication of rules more or less arbitrary

The adoption in the case of precordial leads of symbols different from those employed in the case of the standard leads might have some ad vantages This would however have at the same time tremendous disadvantages It would add an entirely new terminology to clinical electrocardiography which is already regard d by many as an abstruse and incomprehensible subject and would greatly increase the number of technical terms which beginners in this field *would have to learn It would invite* oth r attempts to improve upon electrocardiographic terminology and would stand little chance of prompt and universal acceptanc Th adoption of new symbols for the initial ventricular deflections would greatly complicate the use of such terms as *the P R* interval the QRS interval the RS T segment and the RS T displacement which could not then be logically used in reference to precordial leads For these reasons it was decided that the d flections of the precordial leads should be d signated by the same letters as those of the standard limb lead

In addition to establishing uniformity in the connections for single or multiple precordial leads these recommendations make the interpreta tion of the tracings much easier *since all the waves in the normal chest* leads are upright This also permits the precordial leads to be correctly

designated by the same letters as those of the standard limb leads Lead 4F is the direct lead recommended for routine use (Figs 239 240 241)

While precordial leads display their greatest usefulness in the diagnosis of acute infarction, they are occasionally useful in the study of other con

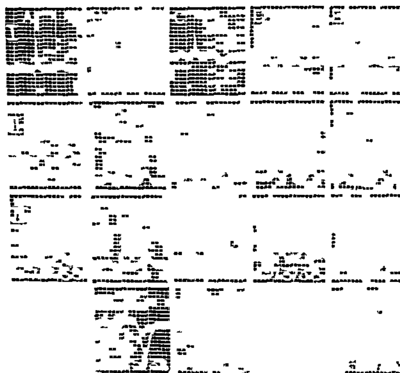


Fig 240 Value of direct lead Patient a foreman of 48 admitted to Receiving Ward of Woman s College Ho pital compla ning of abdominal pain He gave a history of stoma h trouble and ind gestion for five ye r A tentat ve d agnosis of ruptured peptic ulcer w s m de A T ken on adm s ion Ind ect leads no mal B Taken six hours late Th direct lead 4F show change suggest ve of acute infarction (anterior) A slight alte at on may be noted in th RS T interval of the indirect lead C Six days later change n RS T interval n lead 1 more pro iounced D Two months later Evi d nce fad ng from indirect leads D Follow up exam nati n a year later shows no ev dence of presence of area of healed infarct on

ditions For example in the presence of puzzling auricular arrhythmias the P wave may be better visualized in the chest lead For this record the chest electrode is placed over the middle or just to the left of the sternum In making the differential diagnosis between acute coronary occlusion and pulmonary embolism chest leads are helpful while they permit a more complete study of myocardial injuries arising from other causes for ex ample trauma and pericarditis

## DIAGNOSIS OF CORONARY OCCLUSION BY THE RHYTHM OF THE ELECTROCARDIOGRAM

Conduction disturbances are not infrequently observed following acute coronary occlusions Since the bundle of His is supplied by a branch of the

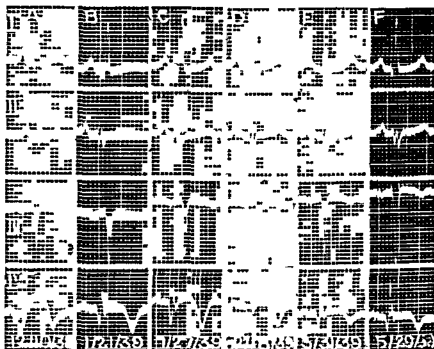


FIG 241 Value of direct lead Patient a salesman of 35 Blood pressure normal Family history positive for coronary disease and angina (both father and mother) A Taken three hours after onset of sharp pain in left shoulder Usual or indirect leads while suggesting the presence of heart disease ( w complex of lead ) failed to show *presence of area of infarction Lead 4F however taken at the same time* shows characteristic monophasic curve While the T waves in leads 1 and 2 of B are flat there is no additional evidence in the indirect leads of the series of the presence of infarct A series of characteristic changes may be seen in lead 4F

right coronary artery posterior occlusions may produce varying degrees of auriculoventricular block Occlusions may also result in block of a bundle branch The rich protective blood supply about the bundle of His and the re establishment of the circulation to this area by collateral flow following the occlusion probably account for the return of normal in rhythm in *Fig 242 The sudden appearance of a cardiac irregularity of this* type with or without chest pain should always suggest the possibility of coronary occlusion The onset of the complete heart block in the patient whose tracing is shown in Fig 243 was attended only by faintness while the patient whose tracing appears in Fig 244 had Adams Stokes seizures

that occurred during the last six hours of life The signs of posterior coronary occlusion usually accompany those of heart block Note the alter

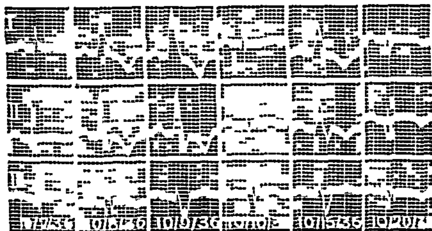


Fig 242 Serial electrocardiographic studies (usual leads) taken over the course of two weeks following an acute coronary occlusion Note the appearance of a bundle branch defect on some days and the return subsequently of normal conduction After four weeks of bed rest the characteristic widening of bundle branch block did not reappear

ation in the RS-T interval in leads 2 and 3 of Fig 243 At times a bundle branch defect may obscure the usual curves of infarction in both indirect and chest leads Consequently in these cases it is hazardous to base a diag

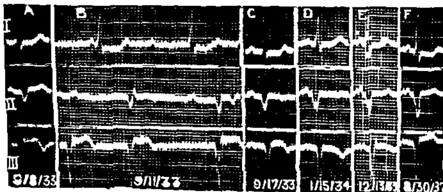



Fig 243 Transient complete heart block following posterior coronary occlusion See Case No 43

nosis on the electrocardiogram However if complete heart block appears suddenly and the clinical picture is suggestive the diagnosis of occlusion

should be suspected An acute coronary occlusion may also usher in a *paroxysm of ventricular tachycardia (Fig 245)*



Fig 244 Electrocardiogram made a few hours after the onset of attack of chest pain Note presence of complete heart block The patient had a series of typical Adams Stokes *seizures and died six hours after this tracing was recorded*

## ELECTROCARDIOGRAPHIC ALTERATIONS FOLLOWING DIGITALIS

As we would expect the electrocardiogram shows marked changes following the administration of digitalis Often these are characteristic of the action of the drug although at times they cannot be distinguished from

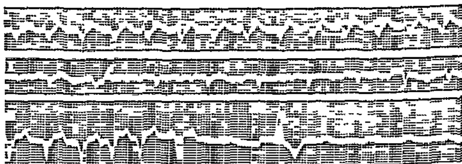


Fig 245 Paroxysmal ventricular tachycardia following onset of initial attack of coronary thrombosis in an Irish janitor of 51 Hypertension present for 10 years The patient died in the receiving ward while this tracing was being recorded

the effects produced by cardiac disease The alterations produced by digitalis in the electrocardiogram are helpful to the physician in directing therapy and may prove of great benefit to patients since electrocardio

graphic changes may serve as warnings of the approach of toxic action Death from overdosage of digitalis is not unknown consequently any laboratory aid in checking the effect of the administration of this drug is an advantage

**P and T Waves** Digitalis affects the heart rate and rhythm It may alter the shape of the P and T waves of the electrocardiogram When the influence of the vagus predominates in the early stages of digitalis action slowing of the heart may be present In toxic amounts digitalis may speed the heart with the production of paroxysms of ventricular tachycardia

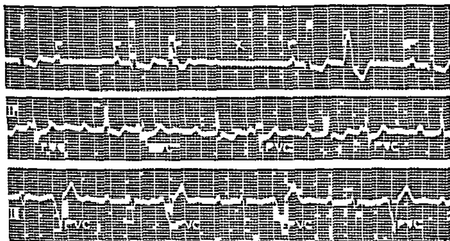


FIG 246 Electrocardiogram of a patient suffering from rheumatic heart disease mitral and aortic stenosis Eighteen grains of the whole leaf of digitalis were administered over the course of the week before above tracing was made Note premature ventricular contractions following normal beats the prolongation of the P R Intervals and the dropped beat at x

**A V dissociation** may be produced by digitalis with slowing of the heart (Fig 246) This is caused by vagal action and is a toxic manifestation Both flutter and fibrillation have been reported following massive doses of digitalis A V nodal rhythm may also appear (see Fig 197)

Varying degrees of heart block may be induced by digitalis when fibrillation of the auricles is present Here digitalis registers its most dramatic effects acting almost as a specific remedy in patients with high ventricular rates (Fig 247)

**Premature Beats** Digitalis frequently produces premature beats in diseased hearts Bigeminal rhythm is a characteristic sign of the toxic action of digitalis (Fig 248) Isolated premature beats should also be considered in the category of warning signs when digitalis is being administered When these are observed if the drug is not properly regulated serious paroxysms of ventricular tachycardia may appear However it must

be kept in mind that the presence of premature contractions alone is not a contraindication to digitalis therapy Many times following successful digitalization this arrhythmia entirely disappears

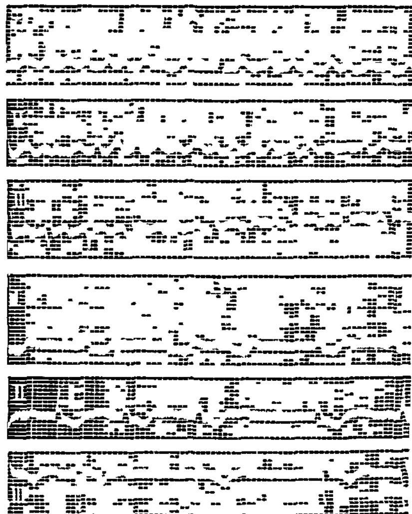


Fig 47 Two three lead electrocardiograms illustrating the effect of digitalis in a patient suffering from rheumatic heart disease and auricular fibrillation A Before digitalis Ventricular rate 170 B Same patient three days later following the administration of 1 3 grams (19½ grains) of whole leaf of digitalis Note the slowing of the ventricular rate in B (8 ) and depression of the S-T Intervals in all leads There was striking clinical improvement

Vagal action is probably responsible for the alteration in the P wave of the electrocardiogram that occurs following toxic doses of digitalis These

changes are encountered most frequently in lead 3 and include all the alterations in the P waves shown in Fig 179 They are however of little clinical significance

T Wave The greatest influence of digitalis is upon the T wave of the electrocardiogram If Figs 247 and 248 are closely inspected the change will be seen to be brought about by a depression of the S-T segment of the tracing This pulls the T wave down with it producing an appearance in the electrocardiogram that is quite typical of the action of digitalis In

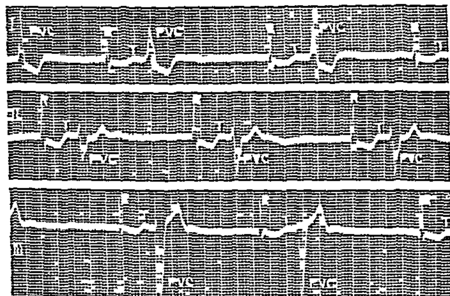


Fig 248 Effect of overdigitalization Pacemaker displaced to A V node (nodal rhythm) Note the premature ventricular contraction following each nodal beat and the depressed S T Intervals

patients with normal hearts and upright T-waves this electrocardiographic change follows the administration of digitalis It may also be observed in patients who have mild myocardial damage In badly damaged hearts however upright T waves may become inverted in a manner not at all characteristic At times the inversion may resemble the coronary type of T wave If the T wave is already inverted by disease the administration of digitalis may cause it to assume an upright position (Fig 249) Consequently interpretations of these changes may lead to false impressions unless the electrocardiographic laboratory is in possession of exact information concerning the amount of digitalis that the patient has received and the date the administration was begun It is likewise important to remember that the laboratory cannot always tell the stage of digitalization by an inspection of the shape of the T wave The change in the T wave reaches

its height while the action of digitalis is still a therapeutic one Continued dosage may produce toxic signs but causes no further change in the T wave

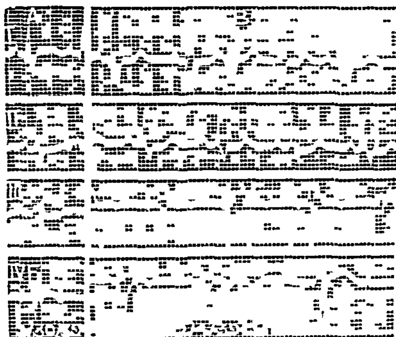


FIG 49 Effect of digitalis on T Wave A Tracing taken during an attack of congestive failure The patient was a woman of 48 suffering from hypertensive cardiovascular disease B Taken after the administration of 1 5 grams (? ½ grains) of the whole leaf of digitalis Note change in T and T In lead 1 of B there is an interpolated premature ventricular contraction There is a slight widening of the QRS groups

## ELECTROCARDIOGRAM IN CHILDREN

While the fundamentals of electrocardiography are essentially the same in adults and children in early life some variations may be observed in the duration and amplitude of the component parts of the electrocardiogram[46, 118]

**P Wave** The duration of the P wave in children should not exceed 0 09 second and the height 0 07 mm Rheumatic heart disease is the common cause of abnormal notching increase in height and widening of the P wave in younger patients Congenital heart disease particularly pulmonary stenosis may increase the height of the P wave but the other alterations are rarely encountered

**P R Intervals** According to Ashman the P R intervals from birth through the fifth year average 0 11 to 0 12 second from ages six to nine 0 12 second, from 10 to 12 0 135 second and for ages 13 and 14 0 14 sec

ond The normal P R intervals in children range from 0 14 to 0 18 second These variations depend on the age and the cardiac rate

**Right axis deviation** is a common finding at birth but tends to disappear in a few months (see Fig 188) Extreme right axis deviation is associated with congenital pulmonary stenosis while a less marked degree of right axis deviation accompanies mitral stenosis

**Left axis deviation** is not as common since the major causes of this shift in the axis are not present in children Coarctation of the aorta aortic regurgitation and stenosis and occasionally uncomplicated mitral regurgitation may produce left axis deviation

**The QRS complex** usually measures 0 06 to 0 08 second and never exceeds 0 09 second in normal records of children Low voltage of the QRS is rare A $Q_3$ wave is not abnormal in the presence of a right axis deviation

Occasionally bundle branch block may be encountered in healthy children The P R intervals in many of these cases are short (0 09 second) and paroxysms of tachycardia are often present An accessory A V bundle (bundle of Kent) has been offered as an explanation of this finding

**The RS T interval** may be elevated in all three leads in the presence of pericarditis in children as well as in adults This elevation must exceed 1 mm before it can be considered abnormal

**The T waves** in lead 1 are usually higher in children than in adults The height of T shows little variation However $T_3$ is not as high in children Congenital malformations tend to increase the height of the T waves

**Sinus arrhythmia** is common in children and is not abnormal Premature beats are rare but may accompany rheumatic heart disease Sometimes they may be observed in the absence of any other evidence of cardiac abnormality Prolongation of the P R interval is a common finding in the presence of rheumatic carditis although higher grades of block are rare Complete block may be congenital (see Case 54) In diphtheria complete heart block may occur and usually points to a poor prognosis Auricular fibrillation or flutter rarely occurs in children When present these arrhythmias complicate either rheumatic heart disease or cardiac failure secondary to a serious congenital defect (see Case 56)

## MISCELLANEOUS ELECTROCARDIOGRAPHIC PATTERNS

### Ventricular Strain

In addition to the great value of electrocardiography in the diagnosis of the various cardiac arrhythmias and acute myocardial infarction it has proved its usefulness in a variety of other conditions For example when either a sudden or chronic strain is placed upon either ventricle significant alterations appear In hypertension the T waves in lead 1 or in leads 1 and 2 may reflect the strain placed on the left ventricle long before the appear

ance of clinical signs of weakness or failure (Fig 250) If the strain is relieved the T waves return to normal (see Fig 121 A and B) It can also be shown by animal experimentation that a sudden right ventricular strain produced by temporarily clamping the pulmonary artery will cause a deep inversion of the T-wave in leads 2 and 3 Similar changes have been ob-

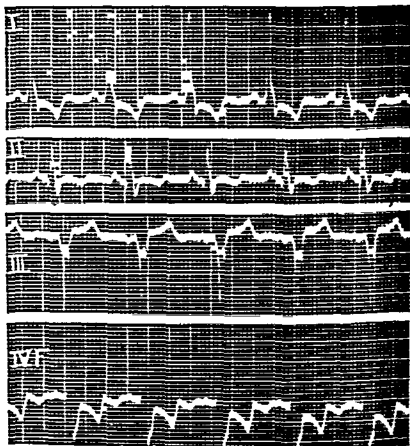



Fig. 250 Electrocardiogram taken on a woman of 6_ with severe hypertension No digitalis had been given No history of anginal or occlusion. Slight cardiac enlargement This tracing shows depressed S-T segments in leads I and 4F This diphasic T is suggestive of chronic left ventricular strain.

served in the human electrocardiogram following acute cor pulmonale (Fig 251) Consequently in many instances the electrocardiogram may distinguish between acute pulmonary embolism and sudden coronary occlusion. Ventricular strain produced by congenital lesions may also be reflected in the T waves of the electrocardiogram

Often the tracings reflecting ventricular strain resemble those produced by block of one of the bundle-branches Barnes[1] has ______ed that the

pattern may be caused by metabolic changes produced by the excessive work placed upon the ventricular muscle Since the presence of fatigue products lessens conductivity and modifies electrical potential some change in the electrocardiogram would be expected

Conditions that commonly place an extra load on the left ventricle are hypertension aortic stenosis and aortic regurgitation As a result of this strain T wave changes and left axis deviation may be observed in the absence of any disease of the coronary arteries Occasionally in the presence of one of the conditions known to produce left ventricular strain signs of right ventricular strain may appear In these instances clinical evidence of mitral stenosis or pulmonary arteriosclerosis should be sought since either of these conditions may exert an influence on the right ventricle Consequently when the electrocardiogram displays an unexpected alteration the clinical evidence should be reviewed Often a satisfactory explanation will be found

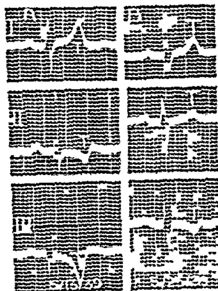


Fig 251 The electrocardiogram in acute right ventricular strain A was taken three hours after the sudden onset of chest pain and hemoptysis in a colored boy of 3 Note S wave in lead 1 the S-T take off below the isoelectric level in leads 2 and 3 and small Q B was taken a week later Note the disappearance of the S wave in lead 1 upright T and decreased depth of T Q has disappeared and there is a deep S wave in lead 3 The diagnosis of pulmonary embolism was made but its site of origin remained a mystery

Left ventricular strain first produces a left axis deviation The R wave in lead 1 is over 12 mm in height while $S_3$ is inverted and measures 5 mm or more below the base line If the strain continues the T wave in lead 1 may become inverted (Fig 250) T may show less marked inversion while $T_3$ has an opposite direction to $T_1$ Atypical tracings appear when other cardiac lesions such as pericarditis acute occlusion or mitral stenosis are present or following the administration of digitalis

Occasionally in patients who show congestive failure secondary to hypertensive cardiovascular disease the blood pressure figure may be normal (page 105) In these instances the typical alterations in the electrocardiogram of left ventricular strain are valuable in suggesting the previous existence of hypertension

Acute right ventricular strain may be produced by pulmonary embolism the degree usually varying in proportion to the size of the artery occluded The S wave in lead 1 of the electrocardiogram becomes deeper

(Fig 251) T may be iso electric, inverted or diphasic If serial tracings are taken $T_2$ will be seen to again become upright $T_3$ is inverted, and a Q wave in lead 3 usually appears The RS T interval in lead 3 in many instances has a cove shape resembling that commonly produced by infarction It must be remembered that all of these changes may not appear in each case Moreover the occlusion of smaller branches of the pulmonary artery produces no electrocardiographic alteration consequently it is always possible for suggestive clinical symptoms to appear without change in the electrocardiogram Barnes [9] has shown that pulmonary infarction complicating the course of acute congestive failure seldom changes the electrocardiographic pattern to any extent, since the emboli in this condition are small and rarely occlude large pulmonary branches As a rule the *greater the degree of shock and circulatory embarrassment following a* pulmonary embolism the more likely it is that confirmatory evidence will appear in the electrocardiographic tracing The changes produced by pulmonary emboli are transient and tend to disappear from the electrocardiogram as soon as the right ventricle recovers from the effect of the sudden strain The exact cause of the production of these electrocardiographic changes is unknown Some observers attribute them to spasm of the coronary vessels of the affected ventricle Barnes believes that they are due to failure of a normal metabolic exchange in the muscle

Congenital pulmonary stenosis and some diseases of the pulmonary vessels and lungs lead to failure of the right ventricle Asthma associated with emphysema and pulmonary hypertension produces the same result Consequently the appearance of the pattern of right ventricular strain in the electrocardiogram in many of these cases comprises valuable additional information The typical electrocardiographic picture of this condition shows a deep S wave in lead 1 and a tall R wave in lead 3 (right axis deviation) $T_1$ is upright T may be positive but is more often diphasic or iso-electric while in long standing cases it is inverted $T_3$ is diphasic or inverted These T-wave changes may be produced by digitalis so it is important to make sure that the drug has not been administered before ascribing them to right ventricular strain

## Pericarditis

The diagnosis of pericarditis at the bedside presents many difficulties (Chapter 4) Consequently the recent recognition and description of electrocardiographic patterns characteristic of this condition have been great aids to the clinician The correct interpretation of these tracings however is only possible when the facts in each case are fully considered

The curves obtained in acute pericarditis resemble closely those produced by an area of infarction Often both conditions may be present simultaneously in which event the changes produced by the pericarditis are superimposed on those of the primary disease

When fluid is present in the pericardial sac it may exert pressure on the coronary vessels producing a myocardial ischemia that is reflected in

the T wave changes of the electrocardiogram[180] The low voltage of the waves of the tracing that is often observed may be caused by the effect of the fluid in the pericardial sac on the electrical impulses[8] Other observers[154 377] believe that the elevation of the RS T segment of the electrocardiogram seen in acute pericarditis is the result of invasion of the subepicardial myocardium by the infectious process with the destruction of small areas of cardiac muscle It is quite likely that the latter change is the essential one in the production of the characteristic pattern observed in this disease (Figs 252 253)

In chronic pericarditis adhesions between the heart and the surrounding structures are unimportant When the layers of pericardium become thickened by scar tissue particularly when subsequently reinforced by calcium depositions the action of the heart may be seriously affected Diastolic filling is lessened Under these circumstances a change appears in the electrocardiogram (Fig 254) Low voltage of the QRS groups is the usual finding and as the condition progresses, this is often accompanied by flattening or inversion of the T waves in all leads

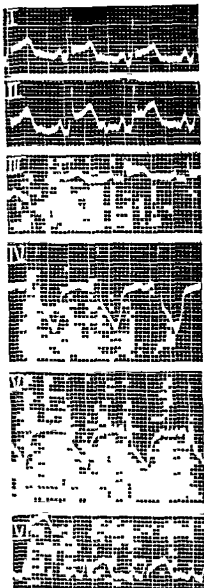


Fig 253 The electrocardiogram in acute pericarditis Note the elevation of the RS T segment in all indirect lead The direct lead in the tracing taken by the old technic (Courtesy of Dr Thomas McMillan)

### Wounds of the Heart

Electrocardiograms following penetrating wounds of the heart may show the presence of pericarditis produced by the incision the escape of blood into the pericardial sac or the infection introduced by the object causing the injury It is possible to distinguish between the electrocardiogram showing damage to the left coronary artery and the tracing produced when pericarditis is the only abnormality present When there is involvement of

the left coronary artery the RS T segment in lead 3 is depressed while the same interval is elevated in lead 1 (Fig 255) When this reciprocal relationship is absent injury to the coronary artery has usually not oc

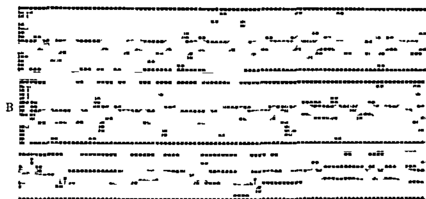



Fig 53 Electrocardiogram of patient of 26 taken during the first week of a febrile illness diagnosed grippe The heart was not enlarged and there were no joint manifestations Note slight elevation RS T segments in all leads The following day a friction rub appeared over the precordium

curred In many instances both effects combine to produce the electrocardiographic change (see Fig 159)

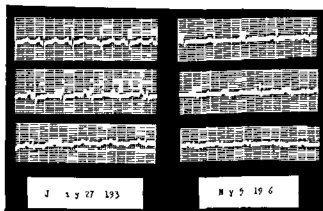



Fig 54 Electrocardiograms taken during the course of development of chronic constrictive (calcific) pericarditis Note change in voltage and flattening of T See Case No 2 page 18

## Diabetes

The electrocardiographic pattern in diabetes is often influenced by the presence of coronary arteriosclerosis Insulin shock associated with hypoglycemia as well as diabetic coma and acidosis produce marked changes in the form of the electrocardiogram Flattened T waves of severe diabetics occasionally become upright and normal when appropriate treatment is in

stituted [94] During insulin shock associated with hypoglycemia the T waves in all leads are decreased in height and in some cases an increase in the A V conduction time has been noted [69]

Diabetic coma produces a depression of the S T interval of the electrocardiogram not unlike that observed following digitalis However in dia

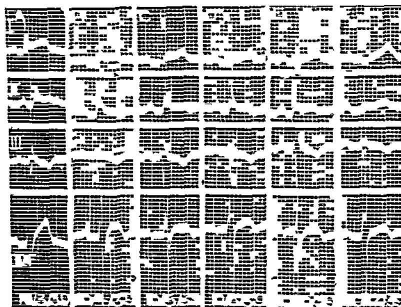


FIG 55 Serial electrocardiograms taken following a stab wound of the left ventricle (ice pick) Note elevation of the RS T segment in lead I of A and the reciprocal depression in lead 3 indicating involvement of the left coronary artery The series of tracings extend over a 10 day period during which time rapid return to normal may be seen Operation was not performed in this case

betic coma the Q T interval is prolonged while digitalis shortens this segment The electrocardiographic changes produced by diabetic coma are reversible Their cause is unknown

## MYXEDEMA

The electrocardiogram in myxedema (see Fig 142C) usually shows low voltage combined with flattening or inversion of the T waves Following treatment with thyroid gland the amplitude of all waves may return to normal Consequently in some cases the electrocardiogram may be of value in differentiating between the changes resulting from myxedema and those due to organic heart disease The characteristic form of the electrocardiogram in myxedema is not produced by alterations in the skin that characterize this condition but is most likely the result of actual myocardial change [1]

# BIBLIOGRAPHY


## A

1 Abbott M E Atlas of Congenital Cardiac Disease American Heart Association 1936

2 Allen E and H Magee Orthostatic Hypotension with Syncope (Ephedrine Therapy) Med Clin N America 18 585 595 1934

3 Allen W B and J W Baylor Influence of Tonsillectomy upon the Course of Rheumatic Fever and Rheumatic Heart Disease Study of 108 Cases, Bull Johns Hopkins Hosp 63 111 1 3 1938

4 Armstrong, E L C B Coggin and H S Hendrickson Spontaneous Arteriovenous Aneurysms of the Thorax a Review of the Literature with a Report of Two Cases, Arch Int Med 63 298 1939

5 Ashman Richard Electrocardiography in Children Modern Concepts of Cardiovascular Disease 7 1 1938

6 Ashman R and E Hull Essentials of Electrocardiography New York Macmillan Company 1937

7 Ayman D Treatment of Arteriolar Hypertension with Crystalline Ovarian Hormone (Theelin) Amer Jour Med Sci 187 806 810, 1934

## B

8 Babcock, W W New Treatment for Thoracic Aneurysm Ann Clin Med 4 933 1926

9 Barach A L Administration of Oxygen by Nasal Catheter Jour Amer Med Asso 93 1550 1551 19 9

10 Barach A L A New Oxygen Tent Jour Amer Med Asso 87 1213 1 15 19 6

11 Barach A L New Type of Oxygen Chamber Jour Clin Invest 2 463-476 19 6

1 Barach A L Therapeutic Use of Oxygen in Heart Disease Arch Int. Med 5 4 8-440 1931

13 Barach A L Treatment of Asphyxia with Special Reference to the Recent Developments in the Use of Oxygen In Heart Disease N Y State Jour Med., 34 67 681 1934

14 Barach A L Use of Helium in the Treatment of Asthma and Obstructive Lesions in the Larynx and Trachea Ann Int Med 9 739 1935

15 Barach A L and R L Levy Oxygen in the Treatment of Acute Occlusion Jour Amer Med Asso 103 1690 1693 1934

16 Barach A L and D W Richard Effects of Treatment with Oxygen in Cardiac Failure Arch Int Med 48 3 5 347 1931

17 Barach A L D W Richards, A T Milhorato, and R. L Levy Effects of Oxygen Therapy on Patients with Congestive Heart Failure Proc Soc Exp Biol and Med 27 308 19 9

18 Barborka C J Treatment by Diet 4th ed. Philadelphia J B Lippincott Company 1939

19 Bardeen C R The Effect of Athletic Sports on the Heart Jour Amer Med Asso 61 1657 1913

0 Barnes A R Diagnostic Electrocardiographic Changes Observed Following Acute Pulmonary Embolism Proc Staff Meet. Mayo Clin 11 11 13 1936

1 Barnes, A R Electrocardiographic Patterns, Springfield Charles C Thomas, 1940

2 Bauer E L Further Studies on the Treatment of Chorea and Rheumatic Infection by Fever Induction Amer Jour Med Sci., 198 24 1939

23 BEAN W B AND C A MILLS Coronary Occlusion Heart Failure and Environmental Temperatures Amer Heart Jour 16 701 1938
4 BECK C S Acute and Chronic Compression of the Heart Amer Heart Jour 14 515 1937
5 BECK C S Surgery of the Heart Trans Coll of Phys Phila 7 3 1939
6 BELL, E T AND B J CLAWSON Primary (Essential) Hypertension Arch Path 5 939 1928
27 BINGER M W AND N M KEITH Effects of Diuretics in Different Types of Edema Jour Amer Med Asso, 101 2009 2016 1933
8 BITZER E W AND G L COOK Clinical Investigation of Incidence of Rheumatic Heart Disease in a Subtropical Climate South Med Jour 27 503 1934
29 BLACKFAN K D AND W HAMILTON Uremia Acute Glomerular Nephritis Cause and Treatment in Children Boston Med and Surg Jour 193 617 1925
30 BLACKMORE A H AND B G KING Electrothermic Coagulation of Aortic Aneurysms Jour Amer Med Asso 111 1821 1938
31 BLAND E F T D JONES AND P D WHITE Disappearance of Physical Signs of Rheumatic Heart Disease Jour Amer Med Asso 107 569 57 1936
3 BLAND E F P D WHITE AND T D JONES The Development of Mitral Stenosis in Young People with a Discussion of the Frequent Misinterpretation of a Middiastolic Murmur At the Cardiac Apex Amer Heart Jour 10 995 1935
33 BLOOM W AND C CASHON Effects of Intravenous Acetyl beta methyl choline on Paroxysmal Flutter Virginia Med Mon 64 341 342 1937
34 BLUMGART H L et al Total Ablation of the Thyroid in Angina Pectoris and Congestive Failure Summary of the Results in Treating Seventy Five Patients during the Last 18 Months Jour Amer Med Asso 104 17 1935
35 BLUMGART H L J E F RISEMAN D DAVIS AND D D BERLIN Therapeutic Effect of Total Ablation of the Normal Thyroid on Congestive Heart Failure and Angina Pectoris Arch Int Med 52 165 1933
36 BOAS E P Cardiac Disorders Accompanying Exophthalmic Goiter Some Factors in their Pathogenesis Jour Amer Med Asso 80 1683 19 3
37 BOOTHBY W M Oxygen Administration Value of High Concentration of Oxygen for Therapy Proc Staff Meet Mayo Clin 13 41 1938
38 BOWER J O AND H A K WERGLE The Additive Effect of Calcium and Digitalis A Warning with a Report of Two Deaths Jour Amer Med Asso 106 1151 1153 1936
39 BRAHDY L AND S KAHN Trauma and Disease Philadelphia Lea and Febiger 1937
40 BRAMS W A J S COLDEN A SANDERS AND L KAPLAN Observations on Toxicity and Clinical Value of Strophanthin Ann Int Med 13 618 1939
41 BRIGHT E F AND C S BECK Nonpenetrating Wounds of the Heart Amer Heart Jour 103 93 1935
4 BRINDLEY P AND F H SCHWAB Aneurysm of the Aorta Findings in 100 Cases at Autopsy Texas State Jour Med 25 757 1930
43 BUCHBINDER W C AND O SAPHIR Heart Failure in Subacute Bacterial Endocarditis Arch Int Med 64 336 1939
44 BUEBLIAN A H Design and Construction of Masks for Oxygen Inhalation Apparatus Proc Staff Meet Mayo Clin 13 654 656 1938
45 BURGESS A M AND F H CHAFFE Oxygen in the Treatment of Coronary Occlusion in the Home New England Jour Med 216 03 05 1937
46 BURNETT C T AND E L TAYLOR Electrocardiograms on 167 Average Healthy Infants and Children Amer Heart Jour 11 185 1936
47 BURWELL C S Influence of Pregnancy on the Course of Heart Disease South Med Jour 29 1194 1936
48 BURWELL, C S W D STRAYHORN D FLECKINGER M B CORLETTI E P

Bowermore and J A Kennedy Circulation during Pregnancy Arch Int Med 62 979, 1938

C

49 Cabot R C Facts on the Heart Philadelphia W B Saunders Co 1936
50 Campbell J A A Box Mask for Administration of Oxygen Brit Med Jour 1 1245 1246 1936
51 Capps J A Subacute Bacterial Endocarditis due to Streptococcus Viridans with Special Reference to Prognosis Ann Int Med 13 280, 1939
52 Carr F B and B E Hamilton Five Hundred Women with Serious Heart Diseases Followed Through Pregnancy and Delivery Amer Jour Obst and Gynec 26 8 4 1933
53 Caughey J L Jr Prolonged Use of Mercurin' Suppositories in the Treatment of Chronic Edema, Jour Amer Med Asso 110 1745 1746 1938
54 Chamberlain F L and R L Levy Clinical Study of a Preparation of Squill (Urginin) in the Treatment of Myocardial Insufficiency Amer Heart Jour 14 68 1937
55 Cheer S N C L Tung and C W Bien Combined Effect of Ephedrine and Atropine on Complete Block Amer Heart Jour 8 400 411 1933
56 Christian H A The Pharmacology of Digitalis in Relation to the Therapy of Heart Disease New Eng Jour Med 208 66 1933
57 Christian H A The Use of Digitalis Other Than in the Treatment of Cardiac Decompensation Jour Amer Med Asso, 100 789 1933
58 Christie, R V *Nasal Mask for Oxygen Administration* Lancet 2 880 88 1938
59 Churchill E D Pericardial Resection in Chronic Constrictive Pericarditis Ann Surg 104 516 529 1936
60 Coburn A F The Factor of Infection in the Rheumatic State Baltimore Williams and Wilkins Co 1931
61 Coburn A F and L V Moore Prophylactic Use of Sulfanilamide in Streptococcal Respiratory Infections with Especial Reference to Rheumatic Fever Jour Clin Invest 18 147 1939
62 Coffey W B and P K Brown *The Surgical Treatment of Angina Pectoris* Arch Int Med 31 00 19 3
63 Coggin C B D E Gripp and W L Stetson Heart in Pneumoconiosis Amer Heart Jour 16 411 1938
64 Cohen M B B S Kline and A M Young The Clinical Diagnosis of Periarteritis Nodosa Jour Amer Med Asso 107 1555 1936
65 Cohn A E and H J Stewart Evidence that Digitalis Influences Contraction of Heart In Man Jour Clin Invest 1 97 125 1924
66 Cole H N Co operative Clinical Studies Syphilitic Cardiovascular Disease *Effect of Specific Therapy on Prophylaxis and Prognosis* Jour Amer Med Asso 108 1861 1866 1937
67 Cole H N Co operative Clinical Studies in Treatment of Syphilis Cardiovascular Syphilis Ven Dis Inform, 17 91 1936
68 Cole H N and L J Usilton Co operative Clinical Studies in the Treatment of Syphilis Cardiovascular Syphilis Uncomplicated Syphilitic Aortitis Arch Int Med 57 893 909 1936
69 Cole H N et al Co-operative Clinical Studies in the Treatment of Syphilis Cardiovascular Syphilis Aneurysm Arch Int Med, 57 919 1936; *also* Ven Dis Inform 17 113 1936
70 Comstock, C R H D Hunt and R S Hayden Value of Cure Regime (with Special Reference to CO Baths in the Treatment of Coronary Disease) N Y State Jour Med 35 715 718 1935
71 Coombs C F Cardiovascular Disease From A Clinical Standpoint; III Rheumatic Heart Disease Clin Jour 62 54 1933

7 COOMBS C F Rheumatic Heart Disease London John Wright and Sons Ltd 19 4
73 CORVISART J N Aphorismes de Med c en Clinique Collected by F V Werat Ed by Paul Bus juet Paris Masson et Cie 19 9
74 CRAIG H R AND P D WHITE Et olory and Symptoms of Neurocirculatory Asthenia Arch Int Med 53 663 1934
75 CRIEP L H Effect of Asthma on the Heart Jour Allergy 2 386, 1931
76 CRILE G W Indications and Contra indications for Denervation of Adrenal Gland Ann Surg 100 667 1934
77 CRILE G W The Surgical Tr atment of Hypertension Philadelphia W B Saunders Co 1938
78 CRILE G W Treatment by Operation on Suprarenal sympathetic System in Neuro circulatory A thenia Tr Sect Surg Gen and Abd Amer Med Asso pp 247 51 1931
79 CRITTENDEN P J AND C IVY A Study of the Viscerocardiac Reflexes Amer Heart Jour 8 507 508 1933
80 CURTIN V T The Problem of the Card ac Child Penna Med Jour 36 168 193

D

81 DOZZI D L Trans nt Nodal Rhy hm Follov ing the Use of Sulphanilamide Amer Jour Med Sc 195 771 1938
8 DRY T AND F WILLIUS Fever Therapy for Subacute Bacterial Endocarditis Proc Staff Meet Mayo Clin 1? 3 1 1937
83 DUBLIN L I AND H H MARKS Mortality of Risks v ith Asthma The Assoc a t on of L fe Insurance Medical Directors of America 1934
84 DYSON J M Pulmonary Heart Disease in Pneumoconios s Amer Heart Jour 9 764 1934

E

85 EASBY M H The Early Recognition of Cardiac Insufficiency in the Presence of Pregnancy Med Cl n N Amer ca 21 1073 1937
86 EASTMAN N J Heart Disease in Pregnancy the Respective Dut es of Intern st and Obstetr c an Med Clin N America 21 1407 1937
87 EDGECOMBE W Stra n of the Heart Pract tioner London 56 87 89 19 1
88 EDMUNDS C W The Potency of D gitalis Preparations of the 1936 Pharma copeia Jour Amer Med Asso 113 84 1939
89 EDWARDS J C AND P D WHITE A N te on the Incid nce of Neurocirculatory Asth n a with and v ithout O gan c Heart Disea e Ne v England Jour Med 211 53 1934
90 EGGLESTON C Drugs Used in the Treatment of Circulatory Failu e in Acute Infectious D seas s Jour Amer Med A so 107 1213 1 15 1936
91 ELKIN D C Diagnosis and Treatment of Wound of the Heart Jour Amer Med Aso 111 1750 1938
9 ELSON JULIUS Free Ball Thrombus of the Left Auricle Amer Heart Jour 10 1 0 1934

F

93 FAHR GEORGE Myxedema Heart A Report B sed upon the Study of 17 Cases of Myxedema Amer Heart Jour 8 91 193
94 FAULKNER J M Th Electrocard ogram in D betic Coma Amer Hea t Jo r 8 691 1933
95 FAULKNER J M Treatment of Cardiov cul r Emergencies New England Jour Med 216 747 751 1937
96 FEIL H AND C S BECK Treatment of Sclerosis and Angina Pectoris by Produc

ing a New Blood Supply to the Heart, Jour Amer Med Asso 109 1781 1786 1937
97 FEIL H AND P L ROSSMAN Electrocardiographic Observations in Cardiac Surgery Ann Int Med, 13 402, 1939
98 FELDMAN L AND I M TRACE Subacute Bacterial Endocarditis Following the Removal of Teeth and Tonsils Ann Int Med 11 2124 1938
99 FENN G K Cardiovascular Disease in the Aged Med Clin N America, 24 23 1940
100 FISHBERG A M Heart Failure Philadelphia Lea and Febiger 1937
101 FISHBERG A M Hypertension and Nephritis Philadelphia Lea and Febiger 1939
102 FITZHUGH T AND C C WOLFERTH Cardiac Improvement Following Gall bladder Surgery Ann Surg 101 478 1935
103 FLEXNER J The Use of the Mercurial Suppository as a Diuretic Ann Int Med 11 11 1938
104 FORMIJNE P *Apnea or Convulsions Following Standstill of the Heart* Amer Heart Jour 15 1 9 1938
105 FOWLER, W M H M HUREVITZ, AND F M SMITH Effect of Theophylline Ethylenediamine on Experimentally Induced Cardiac Infarction in Dogs, Arch Int Med 56 1?42 1935
106 FREIDLANDER R D AND W J KERR The Clinical Diagnosis of Tricuspid Stenosis Amer Heart Jour, 11 357 1936
107 FRIEDMAN M R KLEIN AND P ROSENBLUM Effects of Serum Transfer in Patients with Rheumatic Fever Amer Jour Dis Child 56 1304 1311 1938
108 FRIEDMAN M et al Use of Heparin in Subacute Bacterial Endocarditis Jour Amer Med Asso 113 170 1939
109 FRUEND H A W L ANDERSON AND V S LILLY Recovery from Gonorrheal Endocarditis after Artificial Hyperpyrexia Jour Amer Med Asso 110 549 552 1938
110 FULTON M N Mercurin Suppositories as a Diuretic in the Treatment of Edema New England Jour Med 214 109? 1936

G

111 GAMBLE J L K D BLACKFAN AND B HAMILTON A Study of the Diuretic Action of Acid Producing Salts Jour Clin Invest 1 359 19?5
112 GAY L P *Food Allergy in Internal Medicine with Special Reference to* Paroxysmal Tachycardia and Essential Hypertension Jour Missouri Med Asso 34 33 193
113 GILBERT N C AND G K FENN The Effect of the Purine Base Diuretics on the Coronary Flow Arch Int Med 44 118 1 7 19 9
114 GILCHRIST A Ephedrine Sulphate and Barium Chloride in the Prevention of Stokes Adams Seizures Brit Med Jour 1 610 613 1934
115 GILCHRIST A R AND R M MURRAY LYON Does Pregnancy Hasten the Fatal Termination in Rheumatic Heart Disease? Edinburgh Med Jour 40 587 597 1933
116 GINSBERG A M O O STOLAND AND K A SITER Studies on Coronary Occlusion VI The Effect of Some Members of the Digitalis Group on the Coronary Circulation Amer Heart Jour 16 663 1938
117 GLENDY R F B CASTLEMAN AND P D WHITE Dissecting Aneurysm of the Aorta Amer Heart Jour 13 1 9 1937
118 GLENDY R F AND M M GLENDY Electrocardiography in Infants and Small Children Amer Heart Jour 14 66 1937
119 GOLD H Drug Therapy in Coronary Disease Jour Amer Med Asso 112 1 6 1939
120 *GOLD H, J TRAVELL, AND W MODELL The Effect of Theophylline with*

Ethylenediamine (aminophylline) on the Course of Coronary Infarction following Experimental Coronary Occlusion Amer Heart Jour 14 84 1937

121 GOLDBLATT H Experimental Hypertension Induced by Renal Ischemia The Harvey Lectures 1937 38 pp 237 75 *Reprinted in* Bull New York Acad Med 14 573 1938

122 GOLDBLATT H Experimental Observations on the Pathogenesis of Essential Hypertension Trans and Stud Coll Phys Phila 6 5 1938

123 GOLDBLATT H Experimental Observations on the Surgical Treatment of Hypertension Surgery 4 483 1938

124 GOLDBLATT H Studies on Experimental Hypertension XII The Experimental Production and Pathogenesis of Hypertension due to Renal Ischemia Amer Jour Clin Path 10 40 1940

125 GOLDBLATT H Studies on Experimental Hypertension V The Pathogenesis of Experimental Hypertension due to Renal Ischemia Ann Int Med 11 69 1937

126 GOLDBLATT H Studies on Experimental Hypertension VIII The Production of the Malignant Phase of Hypertension Jour Exp Med 67 809 1938

127 GOLDBLATT H Studies on Experimental Hypertension III The Production of Persistent Hypertension in Monkeys (Macaque) by Renal Ischemia Jour Exp Med 65 671 1937

128 GOLDBLATT H J GROSS AND R F HANZAL Studies on Experimental Hypertension II The Effect of Resection of Splanchnic Nerves on Experimental Renal Ischemia Jour Exp Med 65 233 1937

129 GOLDBLATT H AND J R KAHN Experimental Hypertension Constriction of the Aorta at Various Levels Jour Amer Med Asso 110 686 1938

130 GOLDBLATT H J R KAHN AND R F HANZAL Studies on Experimental Hypertension IX The Effect on Blood Pressure of Constriction of Abdominal Aorta above and below the Site of Origin of both Main Renal Arteries, Jour Exp Med 69 649 1939

131 GOLDBLATT H J LYNCH R F HANZAL, AND W W SUMMERVILLE Studies on Experimental Hypertension I The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia Jour Exp Med 59 347 1934

132 GOLDBLATT H AND W B WARTMEN Studies on Hypertension VI The Effect of Section of Anterior Spinal Nerve Roots on Experimental Hypertension due to Renal Ischemia Jour Exp Med 66 527 1937

133 GOLDEN J S AND W A BRAMS Mechanism of the Toxic Effects from Combined Use of Calcium and Digitalis Ann Int Med 11 1084 1938

134 GOLDMAN L AND A C IVY The Effect of Distention of the Colon and Stimulation of its Nerve Supply on the Flow of Bile from the Liver Ann Surg 110 755 1939

135 GOLDSMITH G A AND F A WILLIUS Body Build and Heredity in Coronary Thrombosis Ann Int Med 10 1181 1937

136 GORDON B The Effect of Exercise on the Circulation and Respiration Jour Med Soc New Jersey 27 672 674 1930

137 GOULEY B A The Evolution of the Parenchymal Lung Lesions in Rheumatic Fever and Their Relationship to Mitral Stenosis and Passive Congestion Amer Jour Med Sci 196 1 1938

138 GOULEY B A The Role of Mitral Stenosis and A Post Rheumatic Pulmonary Fibrosis in the Evolution of Chronic Rheumatic Heart Disease Amer Jour Med Sci 196 11 1938

139 GRAEF I S PARENT W ZITRON AND JOHN WYCKOFF Studies in Rheumatic Fever 1 The Natural Course of Acute Manifestations of Rheumatic Fever Uninfluenced by Specific Therapy Amer Jour Med Sci 185 197 1933

140 GRAYBIEL, A J W STRIEDER, AND N H BOYER An Attempt to Obliterate the

189 KILGORE E Subacute Streptococcus Viridans Endocarditis Failure of Human Immune Transfusion and Serum Therapy Amer Heart Jour 13 619 1937
190 KINSEY DERA AND P D WHITE Fever in Congestive Heart Failure, Arch Int Med 65 163 1940
191 KLEIN T Treatment of Tuberculous Pericarditis with Effusion by Artificial Pneumopericardium Trans Amer Climat and Clin Asso 47 61 1931
19 KNAUER, J G Electrocardiographic Studies on Acute Coronary Thrombosis Ann Int Med 8 1475 1935
193 KOHN C M AND S A LEVINE Evaluation of the Use of Quinidine Sulphate in Persistent Auricular Fibrillation Ann Int Med 8 923 938, 1935
194 KORNS H M Angina Pectoris in a Young Adult Amer Heart Jour 6 423 1931
195 KOUNTZ W B H L ALEXANDER AND M PRINZMETAL The Heart in Emphysema Amer Heart Jour 11 163 1936
196 KRUSEN F AND D ELKIN Fever Therapy for Gonococcemia and Meningococcemia with Associated Endocarditis Two Cases, Proc Staff Meet Mayo Clin 12 3 4 329 1937
197 KURTZ C M Orthodiascopy New York Macmillan Company 1937
198 KURTZ C M ET AL Electrocardiographic Studies during Surgical Anesthesia Jour Amer Med Asso 106 434 1936
199 KURTZ C M AND P D WHITE The Treatment of Subacute Endocarditis by Transfusion from Immune Donors New England Jour Med 200 479 19 9

L

00 LAMB A R Non hemolytic Streptococcus Endocarditis Med Clin N America 2 1077 1919
201 LAMBERT A Action of Autonomic Nervous System as Explanation for Therapeutic Value of Carbonic Acid Baths in Degenerative Cardiac Disease New York State Jour Med 35 147 156 1935
02 LAPLACE L B Relationship of Angina Pectoris to Aortic Valvular Disease Amer Heart Jour 8 810 1933
203 LAWS C L AND SAMUEL A LEVINE Clinical Notes on Rheumatic Heart Disease with Special Reference to the Course of Death Amer Jour Sci 186 383 1933
04 LEAMAN W G JR Congenital Heart Disease Med Clin N America 17 853 1933
205 LEAMAN W G JR The Heart and Athletics Intern Clin 3 1 1934
06 LEAMAN W G, JR History of Electrocardiography Ann Med Hist 8 113 117, 1936
207 LEAMAN W G JR Venous Pressure Its Clinical Importance with a Simplified Technic for Its Determination by the Direct Method Penna Med Jour 38 4 1935
208 LEAMAN W G AND H FOX Observations on Blood Cultures with a Special Reference to the Quantity of Blood Used Jour Lab and Clin Med 12 145 150 19 6
09 LEAMAN W G JR AND S GREENSTON Complete Pulmonary Atresia Report of a Case with Hypertrophy of the Bronchial Arteries Simulating Tetralogy of Fallot New Intern Clin 4 208 1939
10 LEAMAN W G JR AND J S RODMAN Circulatory Problems of Surgical Importance in the Diagnosis of Abdominal Lesions Ann Surg 110 766 1939
211 LEAMAN W G JR AND J S RODMAN Some Differential Diagnostic Problems in the Borderlands of Gastro enterology and Cardiology Rev Gastro enterol 6 366 379 1939
1 LEAMAN W G JR AND J S RODMAN The Surgical Risk with Special Reference to the Cardiovascular System Ann Surg 103 13 1936

13 LEAMAN W G JR AND J H VASTINE, ND Calcification of the Pericardium Amer Jour Roent and Rad Ther 43 35 1940

214 LERICHE R AND A FONTAINE Chirurgie du Sympathique Rev Neurol 1 1046 19 9 *see also* Chirurgie des Nerfs du Coeur Rapport XLI Congress français de Chirurgie Paris, 193

15 LERMAN J R J CLARK AND J H MEANS The Heart in Myxedema Electrocardiograms and Roentgen Ray Measurements Before and After Therapy Ann Int Med., 6 1 51 1 1 1933

16 LEVIN L Angina Pectoris in a Child, Amer Heart Jour 3 495 19 8

17 LEVIN L Cardiac Dyspnoea Its Early Treatment with Mercurial Diuretics Jour Med Soc. New Jersey 33 . 1 11 1936

18 LEVINE S A. Clinical Heart Disease Philadelphia W B Saunders Co 1936

19 LEVINE S A AND W B STEVENS Therapeutic Value of Quinidine in Coronary Thrombosis Complicated by Ventricular Tachycardia Amer Heart Jour 3 53 19 8

2 0 LEVY R. L Diseases of the Coronary Arteries and Cardiac Pain New York Macmillan Company 1936

21 LEVY R. L. Drugs in the Treatment of Heart Disease Ann Int Med 11 1946 1938

LEVY R. L. Some Clinical Features of Coronary Artery Disease Amer Heart Jour., 7 4 1 193

3 LEVY R. L. AND A. L. BARACH Therapeutic Use of Oxygen in Coronary Thrombosis, Jour Amer Med Asso 94 1363 1365 1930

4 LEVY R. L., H G BRUENN AND D KURTZ Facts on Disease of the Coronary Arteries Based on a Survey of the Clinical and Pathologic Records of 762 Cases Amer Jour Med Sci 187 376 1934

5 LEVY R. L., H G BRUENN AND N C RUSSELL JR Use of Electrocardiographic Changes caused by Induced Anoxemia as a Test for Coronary Insufficiency Amer Jour Med Sci 197 241 47 1939

226 LEVY R L AND R GOLDEN Roentgen Therapy of Active Rheumatic Heart Disease A Summary of 11 Years Experience Amer Jour Med Sci 194 597 1937

227 LEWIS, SIR THOMAS Clinical Electrocardiography 6th ed London Shaw and Sons 1937

2 8 LEWIS, SIR THOMAS Diseases of the Heart New York Macmillan Company 1937

2 9 LEWIS SIR THOMAS The Soldier's Heart and Effort Syndrome New York Paul B Hoeber 1919

230 LIBMAN F The Clinical Features of Cases of Subacute Bacterial Endocarditis that have Spontaneously Become Bacteria Free Trans Asso Amer Physicians 28 309 1913

231 LIBMAN F Further Report on Recovery and Recurrence in Subacute Bacterial Endocarditis Trans Asso Amer Physicians 48 44 54 1933

232 LIEBERMAN A L Studies on Calcium; Some Interrelationships of Cardiac Activities of Calcium Gluconate and Scillaren—B Jour Pharmacol and Exp Therap 47 183 192 1933

33 LISA J R AND J F HART Anatomic Observations on 70 Hospital Patients after Sudden Death Arch Int Med 64 43 1939

234 LISTON O Hypertension caused by Food Allergy Jour Missouri Med Asso 34 199 1937

35 LLOYD W D M Dangers of Intravenous Calcium Therapy Brit Med Jour 1 66 664 19 8

236 LONG P H AND E A BLISS The Clinical and Experimental Use of Sulfanilamide Sulfapyridine and Allied Compounds New York Macmillan Company 1939

237 LOVE W S JR The Effectiveness of Trichlorethylene in Preventing Attacks of Angina Pectoris Ann Int Med 10 1187 1937

38 LOVELACE W R JR Oxygen for Therapy and Anesthesia Apparatus for

ministration of Oxygen and Helium by Inhalation Proc Staff Meet Mayo Clin 13 646 654 1938

239 LUCKE B AND M H REA Studies on Aneurysm of the Aorta Jour Amer Med Asso 81 1167 19 3

40 LUETH H C Metrazol in Complete Block with Adams Stokes Syndrome Amer Heart Jour 16 555 560 1938

241 LUTEN, D The Clinical Use of Digitalis Springfield Charles C Thomas 1936

M

242 MCCARTHY P A Treatment of Aneurysms of Thoracic Aaota and Innominate Artery by Distal Arteriovenous Anastomosis Ann Surg 91 161 1930

43 MCCLELLAN W S Balneotherapy in Circulatory Disorders, Arch Phys Ther 15 366 368 1934

44 MCCLELLAN W S Place of CO Baths Internat Clin 1 199 215 1937

45 MCDONALD A L The Aphorisms of Corvisart Ann Med Hist 1 4 1939

46 MCGINN S AND P D WHITE Acute Cor Pulmonale Resulting from Pulmonary Embolism Its Clinical Recognition *Jour Amer Med Asso 104 1473 1935*

47 MCGINN S AND D WHITE Acute Pulmonary Congestion and Cardiac Asthma in Patients with Mitral Stenosis Amer Heart Jour 9 697 1934

248 MCGINN S AND P D WHITE Clinical Observations on Aortic Stenosis Amer Jour Med Sci 188 1 1934

249 MACKENZIE SIR JAMES Angina Pectoris London Oxford Medical Publications Henry Frowde Hodder and Stoughton 1923

250 MACKENZIE SIR JAMES Diseases of the Heart London Shaw and Sons 1913

251 MACKENZIE J Heart Disease and Pregnancy London Oxford Medical Publications 1921

252 MAHER C C AND S G PLECE Multiple Etiological Factors in 5000 Cases of Heart Disease in Chicago Amer Heart Jour 14 490 1937

253 MAHER C C AND P H WOSIKA The Combination of Thyrotoxicosis and Syphilitic Heart Disease Urol and Cutan Rev 43 34 1939

254 MAJOR R H AND L H LEGER Recovery from Subacute Endocarditis following Prontosil (Sulfanilamide Derivative) Therapy Jour Amer Med Asso 111 1919 19 0 1938

255 MARCHETTI R Management of Heart Disease in Pregnancy Med Clin N America 19 893 899 1935

56 MARFAN A B Pericardial Puncture with Particular Reference to Puncture by Epigastric Xiphoid Route Arch Mal Coeur 29 153 178 1936

57 MARRIOTT H L AND K ROBSON Oxygen Administration by Nasal Catheter Brit Med Jour 1 154 157 1936

58 MARTIN H F AND W L ADAMS JR Bacterial Endocarditis Superimposed on Syphilitic Aortitis and Valvulitis Amer Heart Jour 16 714 1938

59 MARZULLO F R AND S FRANCO Myxedema with Multiple Serous Effusions and Cardiac Involvement (Myxedema Heart) Amer Heart Jour 17 368 1939

260 MASSELL B F AND T D JONES Effect of Sulfanilamide on Rheumatic Fever and Chorea New England Jour Med 218 876 878 1938

261 MASTER A M The Electrocardiogram and X Ray Configuration of the Heart Lea and Febiger Philadelphia 1939

62 MASTER A M S DACK AND H L JAFFE Bundle Branch and Intraventricular Block in Acute Coronary Artery Occlusion Amer Heart Jour 16 283 1938

263 MASTER A M S DACK AND H L JAFFE Partial and Complete Heart Block in Acute Coronary Artery Occlusion Amer Jour Med Sci 196 513 1938

64 MALTZ F R Resuscitation of the Heart with Drugs Combined with Electric Shock Proc Soc Exp Biol and Med 36 634 646 1937

65 MAURER F Absence of Pulse in the Vessels of the Upper Extremities and Neck in Aneurysm of the Aortic Arch Amer Heart Jour 17 716 1939

66 MEANS, J H The Thyroid and its Diseases Philadelphia J B Lippincott Company 1937
67 MEININGER, W M AND C W BARNETT Treatment of Syphilis with Sobisminol Mass by Mouth Jour Amer Med Asso, 113 5 1939
268 MIDDLETON W S AND M BURKE Streptococcus Viridans Endocarditis Lenta A Clinico pathologic Analysis of the Experience in Wisconsin General Hospital Amer Jour Med Sci 198 301 1939
69 MIDDLETON W S AND W H OATLAY JR Insulin Shock and the Myocardium Amer Jour Med Sci 181 39 52 1931
270 MAILLAR W Use of Wires in Blood Vessel Surgery Proc Soc Exp Biol and Med 28 193 1930
71 MILLER T G A Consideration of the Clinical Value of Ephedrine Amer Jour Med Sci 170 157 1925
7 MILLS C A Seasonal and Regional Factors in Rheumatic Heart Disease Jour Lab and Clin Med 24 53 60 1938
273 MILLS J H AND B T HORTON Clinical Aspects of Aneurysm Arch Int Med 62 949 1938
274 MOORE J E The Modern Treatment of Syphilis Baltimore Charles C Thomas Co 1933
275 MOORE J E et al Diagnosis of Syphilitic Aortitis Uncomplicated by Aortic Regurgitation or Aneurysm A Comparison of Clinical and Necropsy Observations in 105 Patients Arch Int Med 49 753 1932
76 MOORE, J E J H DANGLADE AND J C RIESINGER Treatment of Syphilitic Cardiovascular Disease Results Obtained in 53 Patients with Aortic Aneurysm and 112 with Aortic Regurgitation Arch Int Med 49 879 9 4 1932

N

277 NATHANSON M H Coronary Disease in 100 Autopsied Diabetics Amer Jour Med Sci 183 495 1932
278 NEYMANN C A Treatment of Disease by Electropyrexia Lancet 1 1102 1935
279 NICHOL, E S Geographic Distribution of Rheumatic Fever and Rheumatic Heart Disease n the Un ted States, Jour Lab and Clin Med 21 588 594 1936
80 NICHOL E S Rheumat c Heart D sease in Southern Florida Amer Heart Jour 9 63 1933
281 NOMENCLATURE AND CRITERIA FOR DIAGNOSIS OF DISEASES OF THE HEART 4th ed New York New York Heart Asso 1939
82 NYLIN J B Physical Exercise in Cardiac Conditions Med Clin N America 20 191 08 1936

O

283 OLD H Asthma from the Life Insurance Standpo nt Jour Allergy 4 1 1933
84 OPPENHEIMER B S AND W M HITZIG Circulatory Measurements in Chronic Lung D sorders Amer Heart Jo r 12 57 1936
285 OPPENHEIMER B S AND W M HITZIG The Use of Circulatory Measurement in Evaluating Pulmonary and Card ac Factors in Chronic Lung Disorders Amer Heart Jour 12 257 1936
86 OPPENHEIMER B S AND H MANN An Electrocard ograph c S gn n Pericard al Effusion Proc Soc Exp Biol and Med 20 431-432 192 1923
287 OPPENHEIMER, B S AND S P SCHWARTZ Paroxysmal Pulmonary Hemorrhages Amer Heart Jour 9 14 1933
288 ORIAS O AND E BRAUN MENENDEZ The Heart Sounds in Normal and Patholog cal Cond tions New York Oxfo d Univ Press 1939
289 OSLER, W Calomel as A D uretic Med News Philadelph a 1887
90 OWEN S E A Study of the V scerocardiac Reflexes Amer Heart Jour 8 496 506 1933

a storage disease, one of the lipoidoses Like hemolytic icterus, it has both clinical symptoms and preclinical laboratory signs The *visible symptoms are characteristic nodules* and tumors of the tendons and joints The laboratory signs consist of increases in the blood cholesterol and cholesterol esters The increases may reach 1500 mg per cent (normal blood cholesterol is 150 to 300 mg per cent) The condition may progress to cardiovascular involvement and sudden death

Since the hypercholesteremia is transmitted on the basis of a dominant hereditary factor and this may be detected by appropriate laboratory tests long before the appearance of visible tumors or nodules, it may profitably be searched for in the relatives of patients with clinical manifestations Where found preventive dietary and other appropriate measures may be instituted

Cases involving dominant genes provide the most striking opportunities for the application of preventive measures on genetic grounds, since the incidence of affected relatives is usually high A dominant gene is one which produces its effect whether it is present upon both or upon only one of the chromosomes of the pair concerned A recessive gene, on the other hand is one which must be present upon both chromosomes of the pair in order to produce its effect Genes occur in alternative pairs, the two members *of a pair being called alleles*

It will be recalled that genes are located in the chromosomes within the cells Since chromosomes occur in pairs in all cells except mature germ cells, genes also occur in pairs in each cell The two members of a pair of genes may be identical, in which case we speak of the individual as being *homozygous* with respect to this particular gene On the other hand the two genes of a pair may be different, due to the individual having inherited a mutated gene (an alternative form of the original gene) In this case the individual is *heterozygous* with respect to this pair of genes Before attempting to make genetic *prognoses, the* physician should have a clear understanding of the differences between dominant and recessive genes and between homozygosity and heterozygosity

### Solution of Medical and Medico-Legal Problems

*The fifth practical* application of genetic principles to medicine involves the medico legal and other medical outcomes of our knowledge of the inheritance of the human blood agglutinogens The number of detectable blood groups has increased in recent years from the original four to more than four million In conjunction with this, there has been an increase in the use of applied genetics *Determination of non paternity*, identification of infants inadvertently interchanged, and identification treatment, and prevention of dyscrasias due to incompatibility between the blood of a fetus and that of its mother are here specifically referred to

### The 'Rh Problem'

The spectacular development and solution of the so-called 'Rh problem' has thrown medical genetics into the forefront of modern medical progress Although maternal fetal incompatibility has important clinical aspects it is primarily a problem of medical genetics and is being solved largely through medico genetic methods Fortunately there are physicians interested in the problem who are well trained in genetics

The problem of maternal fetal incompatibility is a specialized part of the larger problem of the occurrence and inheritance *of human hemagglutinogens Since Landsteiner's* discovery in 1900 of two such agglutinogens, A and B and their combination into four blood groups the problem has continually grown We now know at least twenty five hemagglutinogens in man and these form at least ten series and are capable of combination into more than four million blood groups

### Disputed Paternity

Each of these hemagglutinogens is inherited on a simple Mendelian basis, in such a way that a child never has a specific one of them unless at least one of the parents had it If a child does possess one of these antigens and one of the parents lacks it the other parent must have had it These

facts make it possible to investigate on a scientific basis instances of disputed paternity If a child for example is of group A and the mother is of group O then we know that antigen A in the child must have come from the father If the alleged father should be of group B or group O we can state definitely that he is not the true father of the child Similar medico-legal applications are possible for the other hemagglutinogens (*see* table 44) It is now possible

TABLE 44 —THE MAJOR LAWS PERTAINING TO THE MEDICO LEGAL APPLICATIONS OF THE HUMAN BLOOD GROUPS

1 Hemagglutinogens A B M N P Rh and Hr cannot appear in a child unless they were present in one or both parents

2 Water soluble agglutinogens A and B cannot appear in a child unless one or both parents had the water soluble agglutinogen

3 A parent of group O cannot produce a child of group AB

4 A parent of group AB cannot produce a child of group O

5 A parent of type M cannot produce a child of type N

6 A parent of type N cannot produce a child of type M

7 For any specific Rh Hr factor an Rh negative parent cannot have an Hr negative child

8 Similarly an Hr negative parent cannot produce an Rh negative child

by the use of tests for all the hemagglutinogens, to clear a falsely accused man in well over half the instances

The various agglutinogens occur with diverse frequencies in different populations and follow the laws of population genetics within populations just as they follow the laws of Mendelian genetics within families These hemagglutinogens show varying degrees of antigenicity in man and may or may not have natural antibodies in human individuals Thus the laws of Mendelian genetics population genetics and immunology are jointly responsible for the clinical implications of the blood groups

### KINDS OF HEMAGGLUTINOGENS

Human hemagglutinogens thus far discovered appear to be of three sorts First there are those which are antigenic to man but which are matched by normal antibodies naturally occurring in the serum and other body fluids of individuals not possessing the antigens Such agglutinogens are antigens A and B and the variations of antigen A now known as $A^1$ $A^2$ $A^3$ *etc* Because of the reciprocal presence of natural antibodies against them they are of the utmost importance in transfusions even first transfusions The careful typing of donor and recipient prior to transfusion is now so commonplace as to need no further discussion

Considering antigens $A^1$ A $A^3$ and B there are eight possible blood groups which may result from their combination namely O $A^1$ $A^2$ $A^3$, B $A^1B$ A B and $A^3B$ Moreover these antigens may be soluble only in alcohol or soluble also in water Individuals *having water soluble antigens* are known as 'secretors those not having them are non secretors Since by means of special techniques even individuals of group O may be classified in this way each of the eight *groups mentioned above may be either* secretor or non secretor hence there are sixteen possible combinations

The second kind of human hemagglutinogens are those which have only immune antibodies but which are very weakly *if at* all antigenic to man so that the immune antibodies must be produced by injection of the antigen into animals Such antigens are the agglutinogens M N and P their various subtypes (discovered originally by Landsteiner and Levine in 1927) and presumably also antigen S which modifies the M N types (S was discovered by Walsh and Montgomery and studied by Sanger and Race ) Here the antigens are of little or no clinical importance in transfusion because of the absence of natural antibodies and lack of antigenicity of man but they are of great importance in determination of disputed paternity The application here is similar to that of antigens A and B

The third kind of human hemagglutinogens are made up of antigens which like the second kind have only immune antibodies but which unlike the second kind are at least on occasion highly antigenic to man In such instances immune antibodies are produced by transfusion either

intentional transfusion as a therapeutic measure or unintentional transfusion such as sometimes takes place from an embryo to its mother

At least 14 hemagglutinogens of this sort are known in man These are headed by the antigen originally discovered by Landsteiner and Wiener and named *Rh* Although the original anti Rh antibody was secured through immunization of animals with rhesus monkey blood, it is now known that Rh and similar antigens are antigenic to man and that human immune serums are the best source of antibodies against them

### Rh and Hr

The fact that the original Rh antigen was antigenic to human individuals gave rise to two interesting applications First Although the first transfusion of an Rh-negative recipient with Rh positive blood caused no immediate transfusion reaction, it sometimes did set up the production of antibodies A later transfusion with similar blood might then result in a dangerous reaction in the recipient Second A "transfusion" may sometimes occur across the placenta from an embryo to its mother and cause the stimulation of antibody production in the mother against the Rh factor, if present in the blood of the embryo and lacking in that of the mother The presence of antibodies in the mother's blood may then be dangerous to a subsequent Rh positive fetus This is, of course the explanation of hemolytic disease in the newborn (Levine Katzen, and Burnham, 1941)

The discovery that mothers of children with hemolytic disease frequently had antibodies demonstrable in their serums led to the further discovery that such mothers did not always produce identical antibodies This indicated that various antigens might be concerned with immunization New hemagglutinogens discovered in this way by Wiener were named as varieties of Rh the original Rh being named $Rh_0$, while others were called *rh′ rh″ Rh*$_1$ *Rh* etc Finally, Levine discovered an antibody which identified an antigen reciprocally related to rh′ much as N is to M He called it, appropriately enough *Hr*

All these Rh and Hr antigens were found to be inherited by a child directly from one or both parents The clinical picture therefore is the direct result of a genetic situation which provides the proper setting for immunization These antigens could also be added to the armamentarium for cases involving disputed paternity

### British Rh Research

In addition to active work by American investigators, British workers were participating in the researches on maternal fetal incompatibility Fisher, noting the reciprocal relationship of Levine's Hr to Wiener's rh′, suggested that the Hr factor was only one of a series of such factors and could be called hr′, genetically allelic to rh′ He predicted that $Rh_0$ and rh″ would be found to have similar alleles, which could be called *Hr*$_0$ and *hr″* These were subsequently discovered by Mourant and by Diamond

Race and Fisher have suggested an alternative nomenclature for the Rh factors, one using the letters C, D and E A comparison of the two nomenclatures follows

| *Wiener* | *Fisher Race* |
|---|---|
| rh′ | C |
| Rh$_0$ | D |
| rh″ | E |
| hr′ | c |
| Hr$_0$ | d |
| hr″ | e |

Race and Fisher further postulated that C and c were alleles at a certain locus on a pair of human chromosomes D and d alleles at a closely adjacent locus, and E and e alleles at another closely linked locus Wiener, on the other hand, considers the Rh antigens to be produced by a series of alleles all at the same locus For all practical medical and medico-legal purposes the two hypotheses are the same in the results they give and the question of which is correct is at present largely academic

The British workers have in recent years described several new alternative forms of Rh$_0$ and rh′ These are designated by superscripts—u v w and so on These new hemagglutinogens were discovered after transfusions or maternal immunization and

hence at times may be dangerously antigenic Taking into account these recently described antigens, there are now 15 possible combinations involving the $Rh_0$ series 9 involving rh′ and 3 involving rh″ or 270 Rh Hr groups altogether Since any one of the 640 groups formerly described may also be any one of these 270 there are 172 800 possible combinations

Of all the Rh Hr factors only $Rh_0$ appears to initiate antibody production strongly enough and often enough to be of real clinical significance This antigen is the cause of the antibody formation in almost all the instances of hemolytic disease of the newborn and in almost all of the severe transfusion reactions Since however the other Rh and Hr factors were originally discovered through their occasional clinical manifestations they can not be entirely ignored from a clinical standpoint They are nevertheless of far less significance than antigen $Rh_0$

## New Antigens

In recent years the British workers have described four new antigens discovered in this same way, antigens that seem to be quite independent of one another and of the Rh series Thus far these antigens have been named only for the person who produced the diagnostic antibodies The new hemagglutinogens are the Kell antigen the Lewis antigen the Lutheran antigen and the Levay antigen (*cf* Race 1946 Callender and Race 1946) Since every person must be Kell positive or Kell negative Lewis-positive or Lewis negative and so on and since each such newly discovered antigen thus doubles the previous number of groups it may be seen that the number of blood groups is increasing rapidly Most recently Levine and his associates (1949) have described the Cellano antigen which proves to be an alternative form of the Kell factor so that now each person can be classified as Kell + or Kell + and Cellano + or merely Cellano + Taking into account the Kell Cellano Lewis Lutheran and Levay agglutinogens there are now known 4 147 200 possible distinct blood groups

Of course some of the antigens are exceedingly rare in all populations hence certain combinations of antigens are so improbable as to be practically non-existent

Extension of the work on human hemagglutinogens involves research in active progress at present on the possibility of the effects of immunization other than transfusion reactions and the classical symptoms of erythroblastosis Such effects as blackwater fever as a sequella of malaria congenital anomalies and mental deficiency (for bibliography of current research *see* Snyder 1947 and Snyder and Reinhart 1947) Problems such as these are capable of solution only through the application of the methods of medical genetics

## Value of the Genetic Point of View

Finally it should be mentioned that the employment of the genetic viewpoint by the practicing physician may be expected to benefit not only the physician and his patient but medicine itself For when it is realized that the very early signs of inherited disease so often at present unrecognized or even unknown are to be found more frequently in the relatives of a patient than anywhere else these early signs will be searched for and discovered Slight deviations from the normal deviations which have been ignored in the past by patient and physician alike will take on significant meaning in the light of genetics and the result will be new criteria for diagnosis much earlier identification and consequent new opportunities for prevention

## REFERENCES


Callender S and Race R R 1946 Ann Eugenics *12* 102

Fisher R A and Race R R 1946 Nature *157* 48

Landsteiner K 1900 Zentralbl f Bakt *27* 357

Landsteiner K and Levine P 1927 Proc Soc Exper Biol and Med *24* 291 Jour Immunol *17* 1

Landsteiner K and Wiener A S 1940 Proc Soc Exper Biol and Med *43* 223

Levine P 1943 Jour Pediat *23* 656 1948 Blood the Jour of Hematology Special Issue No *2* 3

Levine P Backer M Wigod M and Ponder R 1949 Science *109* 464

LEVINE P, KATZEN, F and BURNHAM, L, 1941 Jour Amer Med Assn *116* 825

MACKLIN, M T 1933 Jour Assn Amer Med Coll *8* 291 1940 Chap 6 in Medical Genetics and Eugenics Vol I Womens Med Coll of Penna Philadelphia 1941 Sci Month *52* 56

MULLER H J LITTLE C C and SNYDER L H, 1947 Genetics Medicine and Man Cornell Univ Press Ithaca N Y

RACE, R R., 1944 Nature *153* 771, Brit Med Bull *4* 188 1948 Blood the Jour of Hematology, Special Issue No *2* 27 1949 Proc Eighth Int Cong of Genetics 644

SANGER R and RACE R R 1947 Nature *160* 505

SNYDER L H 1941 Medical Genetics Duke Univ Press Durham N C 1943 Chap 2 in Medical Genetics and Eugenics Vol II Womens Med Coll of Penna Philadelphia 1946a Minnesota Med *29*,121, 1946b Bull N Y Acad Med *22* 566 1947a Jour Immunol *56* 281 1947b Yale Jour Biol and Med *19* 817 1948 Trans and Studies, Coll Phys of Phila *16* 116

SNYDER L H and REINHART H L 1947 Ohio State Med Jour *43* 1243

WALSH R J and MONTGOMERY C M 1947, Nature *160* 504

WEINER A S 1943 Blood Groups and Transfusion Charles C Thomas Springfield Ill 1949 Bull N Y Acad Sci *25* 255 1949 Proc Eight Int Cong of Genetics 500

Chapter

# 20

# Psychosomatic Aspects of Medical Practice

BY EDWARD WEISS, M.D.

*Definition.*—*Psychosomatic* is a relatively new term but it describes an approach to medicine as old as the art of healing itself. It is not a new specialty but rather a point of view which applies to all aspects of medicine and surgery. As used in this chapter the term indicates (1) a method of approach to general medical problems which has to do with the simultaneous application of physiologic and psychologic techniques to the study of illness in an effort to make a definitive diagnosis and in preparation for comprehensive medical care; (2) in a more limited sense, reference to a disorder which can be understood only when psychologic as well as physiologic factors are taken into consideration (Halliday). Psychosomatic medicine does not imply studying the *soma less;* it only *implies studying the psyche more.* It is not a new discovery but rather a reaffirmation of the ancient principle that the mind and the body are interactive and interdependent, a principle that has always guided the intelligent general practitioner. Indeed, the traditional old family doctor very often was an excellent psychosomatic physician although he never thought of himself as such. His patients usually were intimate friends and he was familiar with their social situation as well as with their psychologic and physical peculiarities. He was well aware that these factors were related to illness.

As a science, psychosomatic medicine aims at discovering the precise nature of the relationship between the emotional life and bodily illness. Research in the subject is founded on the confluence of modern physiological investigation as developed by laboratory science and animal experimentation and by the discoveries of psychoanalysis, both representing dynamic outgrowths of medicine.

It is the special point of this discussion that psychosomatic techniques of diagnosis and treatment must become an integral part of the practice of medicine in order to fulfill their promise and meet the challenge of present-day medical problems.

*The Organic Tradition in Medicine.*—A great many physicians pride themselves on their unwillingness to concede the absence of physical disease when dealing with an obscure illness. They are apt to say, "But there must be something the matter," meaning that there must be a physical basis for the illness. And they believe that future research will uncover the hidden causes—infectious, allergic, endocrine, or metabolic—responsible for obscure illnesses.

Other physicians are willing to believe that psychic factors have something to do with illness but they have only a vague idea what that something is. These physicians recognize that there is a "neurotic factor" or "a large nervous element" present but they look on this *factor or element as a secondary* one, one probably a consequence of the physical disorder. While freely acknowledging the relation of psychic causes to such physiologic phenomena as blushing, weeping, gooseflesh, vomiting, and diarrhea, they nevertheless find it difficult to believe that more prolonged (chronic) disturbances of a

physiologic nature can possibly be of psychic origin

They are the physicians who often say of a patient that he 'doesn't look neurotic,' perhaps imagining that such a patient should by his general apprehension or by evidences of physical nervousness betray the fact that neurosis is present Their approach to the emotional problem is apt to consist of the question, "Are you worried about anything?' Unfortunately, most neurotics do not betray their neuroses in their appearance, nor is the approach to their emotional problem so simple that the direct question, 'Are you worried about anything?' will produce material of importance

I wish to present the psychosomatic point of view as a practitioner of medicine and not as a psychiatrist, and that is a very different matter When a patient goes to the psychiatrist, he goes prepared to discuss his emotional problems but when he consults a general physician he is almost always looking for a physical cause for his trouble

*Psychosomatic Problems in the Practice of Medicine* —Between the obviously psychotic and the physically ill, are a vast number of sick people who are not 'out of their minds but *have no definite bodily disease to account for their illness* Psychosomatic medicine is chiefly concerned with them (Group I) It is reliably estimated that about *a third* of the patients with chronic illness who consult a physician fall into this group These are the so-called purely 'functional problems of medical practice

Approximately *another third* of the patients with chronic illness who consult a physician have *symptoms that are in part dependent upon emotional factors* even though organic findings are present (Group II) This second group is even more important than the first from the standpoint of diagnosis and treatment For here the psychosomatic problems are often complicated, and, because serious organic *disease may be present the* psychic factor is capable of doing more damage here than it is in the first group

Group III embraces a group of disorders generally considered wholly within the realm of "physical disease, disorders having to do with the vegetative nervous system, such as *migraine asthma* and *essential hypertension* Psychosomatic medicine is much interested in these because it believes that the psychic factor may be of great importance in their etiology and of even more importance, in their management

Here we touch upon a fourth problem, in which studies are just beginning to be made, that is the possible relationship of psychological disturbances *to structural alteration* The point of view toward disease bequeathed to us from the nineteenth century may be expressed in the following formula

Cellular disease→structural alteration→physiological (or functional) disturbance

In the twentieth century this formula has undergone alterations in some situations For example, for essential hypertension and vascular disease, the formula has been altered *to read*

Functional disturbance→cellular disease →structural alteration

We are still in the dark, however, about what precedes the functional disturbance, but future investigations may show us that it is a psychological disturbance Then the formula would read

Psychological disturbance→functional impairment→cellular disease→structural alteration

## PSYCHOSOMATIC DIAGNOSIS

Psychosomatic diagnosis depends much more on case history than on physical examination or laboratory study The diagnosis of a 'psychosomatic affection can only be established by positive data from a psychological standpoint *in addition* to an evaluation of the part that physiological and "organic factors play

In our approach to illness, Halliday tells us that we must ask ourselves these questions (1) What *kind* of person are we dealing with (inherited and acquired characteristics physical and psychologic)? (2) What has *he met (germs* allergens or emotionally disturbing events)? (3) What has *happened* (the physiologic mechanism or pathogenesis of the disorder)? For example allergic responses occur when a prepared organism, possessing certain physical and psychologic characteristics, meets certain elements physiologic and psychologic In some allergic

disorders a single preponderant factor may be largely responsible as for example in pollen hay fever In others such as asthma there are frequently multiple interrelated factors allergens and emotional disturbances which act in a complementary fashion to produce the disorder

In psychosomatic medicine the means of investigation are therefore two—physical and psychologic their simultaneous application represents psychosomatic diagnosis The physician in his usual approach to the patient makes many intuitive observations about the mental processes of the patient What is here suggested is that order be brought into this intuitive process In the psychosomatic case we try to establish the following

1) family history (heredity and pseudo heredity) that suggests a background for psychological difficulties
2) evidence of childhood neurosis
3) sensitivity to specific emotional factors (temporal relationship of present illness and emotionally disturbing event) especially at epochal or crucial life periods (puberty marriage childbirth climacteric etc)
4) specific personality structure (other evidence of neurosis or character disturbance)
5) demonstration of specific behavior on taking the history (artificial exposure to a conflict situation)
6) hyposensitization by psychotherapy or the avoidance of the provocative situation

1 *Family History that Suggests a Background for Psychological Difficulties* —What is often attributed to heredity is in fact pseudo heredity that is acquired as a result of environmental influences It is difficult to distinguish between the effects of the two Unconscious identification for example with a sick parent or a parent figure is an important cause of psychoneurotic and psychosomatic disturbances

2 *Evidences of Childhood Neurosis* —Evidences of childhood neurosis will often be missing—neither the adult patient nor his family can recall his childhood indications of disturbed behavior or bodily dysfunction Nevertheless it is well known that almost invariably, disturbed behavior or psychosomatic illness in adult life is preceded by illness of emotional origin in childhood

The fact that every child shows some evidence of disturbed behavior or disorder of emotional origin complicates the problem It is a question of degree Physicians often say "The child will grow out of it And so he may seem to do but the nucleus of the disorder remains and may manifest itself later in life with a more severe illness Apparently adolescence is the crucial period the period in which the emotional disorders of childhood are either submerged or undergo recrudescence

3 *Sensitivity to Specific Emotional Factors* —When we ask ourselves why a psychosomatic disorder begins at a particular time we must investigate the patient s life at that time in order to discover what events have emotionally disturbed him We know that such events are apt to occur at certain epochs in life such as puberty marriage childbirth climacteric and old age If the patient is not well adjusted the incident that precipitates illness may be trivial if he is well adjusted it may require a major event to disturb him or precipitate a psychosomatic affection In either event the incident is related to his personality structure

4 *Specific Personality Structure* —Almost never does a symptom of emotional origin exist without other evidences of personality disturbances either in the mental or the physical sphere Both cross section and longitudinal studies of the emotional life will show characteristic personality trends which indicate the predisposition toward certain behavior manifestations or to a particular type of disorder For example the hysterical personality may show conversion symptoms while the compulsive personality is apt to have vegetative organ neurosis (asthma hypertension)

5 *Demonstration of Specific Behavior* —When meaningful material is touched upon in taking the history the evidence in the patient s behavior is unmistakable We must of course allow for the stress incident to the first contact between the patient and the physician but usually there is no difficulty in determining from the patient s behavior that a specific vulnerability exists

when certain subjects are broached The process is like the dentist's searching for cavities with his sharp-pointed instrument Defects in the emotional make up must be found, the experienced interviewer discovers them, yet avoids giving pain

*6 Hyposensitization by Psychotherapy or the Avoidance of Provocative Situations* — That a patient improves by means of psychotherapy may be much more obvious to the physician and to the family than to the patient Indeed the patient will often deny that he is better while members of his family attest to his improvement One often obtains a better impression from what the patient does than from the way he says he feels It is better to ask the patient, "What have you done?" rather than "How do you feel?"

Improvement of the environment may also bring about improvement in a great many instances This is the area in which the social worker can be helpful Failure to improve when the environment is improved is in itself an indication for psychotherapy One must be very cautious however about attributing improvement to psychotherapy often something in the patient s environment changes for the better without the physician s knowing it

A special point needs emphasis here since neurosis or psychosomatic illness usually does not first appear in middle life what may seem psychosomatic in the middle-aged patient is often organic

So far as allergy is concerned, the fact that the removal of an allergen or a hyposensitization process cures the patient proves only that one factor has been removed the morbid chain of events interrupted exactly the same reasoning can be applied to psychological factors

Heredity is often held responsible for illness that arises from the environment This is a very important consideration to which too little reference has been made Children identify themselves with their parents and unconsciously imitate them, in this way patterns of behavior are laid down (which include illness as an aspect of behavior) so early in life that we often attribute a disorder to heredity when it is in fact an acquired disorder A final solution to this involved question can hardly be hoped for, for it is not likely that constitutional and environmental factors can ever be separated with absolute precision But unconscious identification with a sick parent or other members of the household in early childhood is very often the basis for an illness later in life which we may attribute wholly to heredity

*Body Language* —Body language is a very satisfactory explanation and approach to many medical problems It has been suggested that the most satisfactory way to deal with tension is by action the least satisfactory by thought in between is speech In other words in all people with psychosomatic illness there is some impairment of total functioning and very often a great deal of energy is wasted on fantasies If we can get such people to talk about their problems we can often understand the illness better and at the same time provide some measure of relief Such patients are like engines with the steam up if the wheels do not go 'round in productive work and the whistle is not blown in talking about their troubles the steam will try to get out somehow and will make an effort to part their seams It is a homely explanation which people readily grasp as they realize that this short circuiting of energy is capable of disturbing their bodily functions If psychosomatic patients cannot express their tension by work or action, if they cannot explain in words what is disturbing them then one of their organs will try to say it for them Thus the patient with nausea who has no evidence of organic disease may be indicating that he cannot "stomach" certain situations, the patient with an itch often "lets things get under his skin" Many additional examples could be given to show that the patient often expresses himself in the symbolic formulas of body language if we would only listen to him (Weiss and English)

Another very satisfactory way to get people to discuss themselves in relation to their illness is to use a case illustration This is often effective when other methods of trying to make people see the relationship between the emotions and illness fail If one can think of an apt case illustration the patient can readily identify himself with it

even where there are marked divergences the patient will often see a partial application to himself which will encourage him to talk about his personal life Sometimes he *will deny the application but then go on to* discuss emotional factors of importance in his own case factors he had been unable think of before

*Taking the Case History* —An important element of the doctor patient relationship enters into the taking of the case history The doctor must listen to the patient uncritically Sympathy for patients suffering *from illness of emotional origin is an es*sential part of the equipment of the physician who would *interest himself in psycho*somatic problems If he is unsympathetic it will show and will discourage the patient from exposing the feelings essential to an understanding of the problem

A physician s ability to use the psychosomatic approach also depends on his knowledge of psychopathology and tissue pathology applied simultaneously His human understanding his sensitivity and sympathetic appreciation of emotional factors as a cause of illness as well as his orientation and experience are all important in determining his ability to deal with psychosomatic problems

Experience of course is important in history taking but even if a *doctor has* practiced medicine for 50 years he will still have to give time to the patient There are no short cuts in history taking though an experienced doctor may quickly grasp the patient s problem he must nevertheless remember that the patient cannot be hurried

The revered family doctor of the small community used his knowledge of his patients personal lives to evaluate their case histories He knew everything that was going on and had a background of understanding gained from personal observation Now in our elaborate medical institutions with a lack of knowledge of the patient s background we over-emphasize the so called scientific aspects of medicine and relegate to the background the social and emotional factors that may enter into illness As a consequence our methods of history taking have not kept pace with other methods in medical science

The body is still divided into many organs and systems specialists look upon disease *from their own narrow points of* view and the curriculum is built up by introducing more and more special points of view As a consequence the comprehensive point of view so necessary to the study of illness as an aspect of behavior can make little headway The medical history form we give our medical students reflects this organic approach and this age of specialization *we look in vain through a long history* for some evidence of the human being who is sick *If patients were allowed to talk more* and were examined less it would be a good thing for medicine in general A patient who had been through the mill of medical investigation recently remarked that she was suffering from testitis How many patients have been examined again and again (by means of $x$ ray chemical studies and various other expensive and complicated methods) with a harmful rather than helpful result because the diagnosis was obscured by concentration on a part rather than on the whole?

Most people who consult a general physician wish to *find some physical cause for* their ailments and so fall readily into the system of answering specific questions about physical health and volunteering no information about themselves as persons Moreover people look upon the physician as an authoritarian figure who will do something about their illnesses and are usually quite unprepared to have to do something for themselves—in other words discuss themselves as persons as well as medical cases *We must look for the person in the* patient Frequently the patient who insists *that his illness is physical is suffering from a* disorder of emotional origin whereas the patient who is eager to blame the psyche for his trouble often has an organic disease Many people seriously sick with advanced organic disease seek to delude themselves with the idea that it may be all mental This applies especially to the many lay persons who have now read some of the *popular writings on psychosomatic medicine*

Psychosomatic medicine requires greater awareness of the emotions in illness and hence more emphasis on certain aspects of history taking More attention must be paid to the behavior of the patient to the words he uses in describing his complaints, to the asides and apparent irrelevancies that so often give important clues to the emotional factor in the case The physician must give the patient time allow him to talk with as few interruptions as possible Extensive notetaking must be avoided so that the patient may feel that the doctor is more interested in him as a person than as a case Interest in what the patient himself sometimes regards as trivial or silly is important, as is close attention to the chronologic development of the life history with special emphasis on the various factors in the childhood period that may have influenced the development of the personality Special attention should be given to puberty and adolescence with their frequent emotional problems and to the epochs and crucial periods in life when psychosomatic disturbances are apt to arise The health of the spouse should be inquired about, neurotics have a way of attracting one another And as complete a picture of the family background as possible should be obtained

*Chronologic Development of Life History* — There are two main approaches to the study of the patient with suspected psychosomatic disorder a *cross section* study of his personality as he appears at the time of the interview, and a *longitudinal* survey of his life from family background and early infancy to the present time The first approach, the cross sectional viewpoint is combined with the story of the present illness It is the traditional approach of the physician to his patient and the only requirement from the psychosomatic point of view is that the social and psychologic aspects of the case be developed in order to show the relationship between the life situation and the medical illness

The cross section approach tries to relate the present illness and the precipitating emotional factor The longitudinal study relates personality development and the past medical history It gives a better idea of the personality structure and psychopathology because it shows the background and the development of the personality One technique does not exclude the other On the contrary, the data derived are complementary and help make up a definitive psychosomatic diagnosis

## PSYCHOTHERAPY

Patients do not have to be told that they are undergoing psychotherapy What we must do can be done in the usual doctor patient relationship

1) After a medical history, which takes account of personal factors as well as "medical facts,' we should make a complete physical examination and such laboratory tests as are necessary to exclude physical disease or establish the precise nature of the organic problem and the amount of disability which it in itself is capable of causing
2) Having assured the patient that there is no physical disease or that disability is out of proportion to the disease it is usually easy, by giving examples of psychic causes for such physiological disturbances as blushing gooseflesh, palpitation, and diarrhea to make the patient understand that a disturbance in his emotional life may be responsible for the symptom
3) The more one can persuade the patient to talk about his other troubles the sooner do we come to an understanding of the present troubles The greater our success in switching the conversation from symptoms to personal affairs the sooner do we come into possession of the real problem disturbing the patient Encourage him to talk about himself as a person rather than as a medical case

Usually one or more of three special fears are uppermost in the mind of such a patient One of the most common is fear of *cancer*, cancerphobia A great many patients think they have cancer and indeed most women who consult physicians will have the idea

at some time They do not always express it in fact they rarely directly express their cancer fear They often disguise it by a complaint about a lump a swelling or a curious sensation in the abdomen or breast and when they are assured at the end of a complete physical examination that they are free from organic disease they heave a sigh of relief and say Oh I am so glad because I thought I might have a cancer

Another common fear is fear of *heart* disease When pain in the precordial region rapid beating of the heart breathlessness and fatigue occur suspicion of heart disease often arises If we remember that the pain of cardiac neurosis bears no definite relation ship to effort is frequently described as sticking needlelike or soreness is often associated with inframammary tenderness and hyperalgesia so that the pressure of the stethoscope sometimes elicits it and may be accompanied by a sense of choking as well as by sighing respirations we shall have no difficulty in making the differential diagnosis if we associate these symptoms with the whole picture and life situation of the patient with cardiac neurosis

The problem is not an easy one for the patient is apt to insist that there must be something the matter He cannot under stand how so much distress can occur unless some vital organ is seriously affected Moreover even if he is reassured for the time being he may nevertheless wonder how long his heart can stand what he considers the strain Telling the patient to control him self is like trying to hold back steam under pressure—if it doesn t come out the spout it tries to blow the lid off the tea kettle It does no good to try to persuade him that he does not have physical disease you cannot argue with an obsession One must get at the mixed feelings at the conflict that under lies the anxiety and this can only be done by *encouraging the patient to talk about his* personal problems This discussion will usually have to do with the family group For example in a young married woman caring for a sick mother respect and devo tion were opposed to inner resentment over the effort and cost and the disruption of her own family life this led to an anxiety which could not be dealt with by mere reassurance regarding the absence of organic disease lectures on self-control and the admin istration of phenobarbital

The inability to concentrate often gives rise to a fear of ' losing the mind This fear is frequently associated with ideas of *suicide* Both are very distressing to the patient and usually are not volunteered But when the patient is assured that it is his feelings which are involved and not his mind and that the reason his memory fails him is that he is so preoccupied with his problems he may confess his fear of losing his mind and his thoughts of doing away with himself

Once these ideas are brought to the surface and ventilated and the patient receives sufficient reassurance much improvement often occurs Indeed the intensity of the fear and the amount of reassurance necessary to abolish it are a crude index of the depth of the neurosis

It is a good rule to listen rather than talk Giving advice on highly charged emotional matters is dangerous To paraphrase Lindemann Clumsy psychotherapy is as danger ous to the social life as clumsy surgery is to the physical life

One more point should be emphasized—the *gastrointestinal tract* is above all other systems the pathway through which emotions are often expressed in behavior Why this is so becomes apparent when we con sider that the infant s first contact with the world is through the mouth so that the processes of feeding and feeling must relate themselves to one another Therefore upon the love and security or anxiety and insecurity which become associated with the nursing process will depend many of the psychosomatic relationships of adult life called forth by events which awaken old associations Truly it can be said that bed and board are as indissolubly related in the *life of the adult as are sucking and sensuality* in the life of the infant

*The Anxiety Attack* —Frequently the first pronounced evidence of neurosis is an anxiety attack The patient experiences a feeling of weakness sweating and a sensa tion that something terrible is about to happen He suffers from dyspnea palpita tion and sometimes nausea The attacks

usually last only a few minutes and subside rather quickly but may last for an hour or more. Weakness and fatigue follow. The emotional as well as the physical distress is so marked as to cause the patient to conclude that some very serious physical disability is present. Almost never does he conclude that his difficulty is emotional. Most people prefer to think that physical distress means physical disease and, unfortunately, physicians too frequently have assisted them in this belief. When a patient with an acute anxiety attack is first examined, the physician notes the rapid pulse and listens to the pounding heart and all too often permits the patient to believe that the heart is diseased, that hyperthyroidism is present, or covers his unwillingness to make a diagnosis of a psychological disorder by using some such term as neurocirculatory asthenia or autonomic imbalance. To give drugs and do nothing about fear is to mislead the patient into feeling that his distress is due to a physical disease rather than to an emotional disorder.

*Marriage and Parenthood as 'Cures.'*—It is not unusual for physicians to recommend pregnancy and parenthood as a cure for neurotic and psychosomatic illness. This prescription is rarely, if ever, of value. It is a pretty safe rule that the unstable person will not be helped by becoming a parent but will usually be made worse as a result of the added responsibility. How often upon taking the history of neurotic persons, especially women, do we hear, "I was perfectly well until my first child was born but I haven't had a well day since." It is true that some neurotic women will feel better during pregnancy but they pay dearly for their short period of improvement. Nor should the cost to the child be forgotten. Not only does parenthood not cure neurosis but it prepares the way for another spoiled life, for this is surely one of the ways in which neurosis is perpetuated. The atmosphere of the home in which there is serious emotional maladjustment creates the culture medium for the development of further emotional problems. This is the real social disease. Psychological contagion is as important as germs in causing illness. The advice to an incompatible couple—"What you need is a child, then you will have a common interest"—is as unenlightened as it is dangerous. While it may succeed in holding the marriage together, who can say how many children are thus sacrificed on the altar of incompatibility?

*Sexual Factors.*—Ever since the introduction of the epoch making studies of Freud to the problems of neurosis, medicine has misunderstood his conception of sexuality. He has often been quoted to the effect that disturbances in genital activity are the sole cause of the neuroses. This is very far from the truth. It is rather that difficulty in the sexual sphere appears as a revealing index to a neurotic personality and can be looked upon in that light. In other words, in much the same manner that urea retention serves as an index to an impending uremia, so do disturbances in the sexual life of the individual, such as varying degrees of frigidity in the female and varying degrees of impotence in the male, serve as a reliable index to the kind of personality that is very apt to develop a neurosis. Sexual difficulties are rarely in themselves the cause of the kind of illness under consideration. When they are important and the patient has a satisfactory relationship to the physician, sufficient confidence will eventually be gained to permit discussion of these intimate matters. In women, questions regarding menstruation and childbearing will often lead naturally to such a discussion.

In this connection let us suggest a *cautious attitude in regard to marital maladjustments* which are often in the background of obscure illness. The better these problems are understood from the standpoint of personality study, the clearer it becomes that serious emotional maladjustment is behind the marital problem. Consequently, casually to give advice regarding marriage and childbearing, divorce and extramarital relationships as short cuts to involved emotional problems is to assume knowledge beyond present human understanding.

*The Aims of Psychotherapy.*—And now to come to one of the questions frequently raised by physicians regarding these matters. Suppose you *do* find something of importance in the emotional life of a patient, some conflict that is causing illness—what good does it do the patient to know? What can you do about it?

First of all it is often a great help to the patient to know that the ailment is not organic in origin but is due to a disturbance in his emotional life *When a neurotic symptom is divorced from a fear of organic disease—cancer for example—it loses its force whereupon the slogan carry on in spite of symptoms often helps the patient a great deal* This is especially true if the psychological approach which we have discussed is combined with the case study and the emotional background of the illness is made clear to the patient

*Major and Minor Psychotherapy* —A considerable number of the patients whom we have been considering cannot be sent to psychiatrists nor is it necessary Not that there is anything reprehensible about consulting a psychiatrist—this too is a problem of education—but there are not enough psychiatrists to take care of the thousands of patients Moreover a great part of the work lies in the field of general medicine The general physician must be able to treat the minor ailments but he must also recognize when the problem is beyond him and then refer his patient elsewhere for major psychotherapy Such knowledge and such an approach frequently will save the patient from unnecessary troublesome and expensive medical or surgical treatment with a resulting further degree of invalidism

*Cost of Psychotherapy* —What about the question of time effort and the expense of psychotherapy? All this takes time and effort and must be paid for yet when we look into the time effort and expense that have been expended by many patients or by institutions taking care of these patients in the usual medical approach we realize that an hour or two well spent in a discussion of the life situation of such patients would obviate a great deal of this expense

What indeed, is psychotherapy? Too often it is assumed to be something vaguely referred to as the application of the art of medicine This defies analysis but seems to represent a combination of the experience and common sense of the seasoned practitioner an intuitive knowledge of people the cultivation of a charming bedside manner such trifles as serving food in attractive dishes, and the generous use of sedatives placebos and reassurance The psychological approach in medicine essential for psychotherapy consists of something more It is a medical discipline to an equal degree with internal medicine itself It is an effort to understand the personality structure of patients the mental mechanisms which are at work and the specific relationships of psychological situations in the precipitation of the illness

Reassurance in the majority of instances unless combined with an analysis of the illness from the standpoint of the behavior gives only temporary help and depending upon the degree of anxiety has to be repeated constantly like a dose of digitalis to a failing heart *Closely allied to reassurance* is another superficial treatment that rarely results in more than temporary help *i e* environmental manipulation without any attempt to give the patient insight into his conflicts

Real psychotherapy which is directly the opposite of simple reassurance tries to make the patient understand the meaning of his symptoms and the nature of his conflicts It is a process of re-education and when properly done leads to sufficient emotional development so that the necessity for symptom formation is abolished The best example of this kind of psychotherapy is psychoanalysis but for various reasons this method cannot be applied directly to the majority of patients Nevertheless psychoanalytic insight and guidance prove adequate to handle the emotional factor in the majority of psychosomatic disturbances Between simple reassurance at one end of the scale and adequate psychoanalysis at the other there are all degrees of psychotherapy which can be applied depending upon the degree of illness and circumstances of the patient

## REFERENCES

Halliday J L Principles of Etiology Brit Jour Med Psych 1943 *19* 367

Kubie L S Review of Human Constitution in Clinical Medicine Psychoanal Quart 1944 *13* 503

Lindemann E Therapeutic Procedures in Psychoneurosis New Eng J Med 1942 *227* 584

Weiss E and English O S Psychosomatic Medicine 2nd edit W B Saunders and Co Philadelphia 1949

# Chapter 21

# Diseases of the Heart

By SAMUEL BELLET M D and ARTHUR BERNSTEIN M D *

## CLASSIFICATION OF HEART DISEASE

The classification of the American Heart Association has been widely used Though it has certain definite drawbacks and is subject to a certain amount of criticism, it *has done much to promote comprehensive* thinking and has helped standardize discussion of the various problems According to these standards, a complete diagnosis consists of five divisions

A Etiologic (rheumatic fever, arteriosclerosis etc )

B Anatomic (infarct of myocardium etc )

C Physiologic
   Cardiac mechanism (normal sinus rhythm auricular fibrillation)
   *Clinical syndrome* (anginal syndrome paroxysmal dyspnea)

D Functional
   Class I (no discomfort on ordinary physical activity)
   Class II (some limitation of activity some discomfort on activity)
   Class III (increased limitation of activity discomfort on less than ordinary activity)
   Class IV (discomfort on all activity)

E Therapeutic
   Class A (ordinary physical activity needs no restriction)
   Class B (severe or competitive efforts must be forbidden)
   Class C (ordinary activity needs moderate restrictions, *strenuous habitual* efforts must be forbidden)
   Class D (ordinary activity needs marked restriction)
   Class E (complete bed rest required)

There are two further categories potential heart disease and possible heart disease A sample diagnosis follows

A Rheumatic Heart Disease (arrested)

B Enlarged left auricle left ventricle right ventricle and right auricle
   Aortic insufficiency, mitral stenosis mitral insufficiency

C Auricular fibrillation Paroxysmal pulmonary edema

D Class IV

E *Class I*

*Etiologic Types —Rheumatic Heart Disease* —This is one of the most important forms of heart disease and is largely responsible for cardiac disability during early life

*Other Types of Cardiac Infection* —Certain other types of infection are occasionally responsible for cardiac damage In serious and fatal cases of diphtheria the myocardium may be extensively injured by the toxin Scarlet fever is at times complicated by an endocarditis or pericarditis The cardiac involvement in some cases particularly those with arthritis has been attributed to

* This chapter was originally written by the late Fred M Smith M D and has been revised and largely re-written by the above authors Doctors G D Geckeler B A Gouley W C Leaman and W Lekoff have written the section The Heart in Special Conditions

an associated rheumatic infection In rare instances endocarditis has followed measles and whooping cough Other bacterial or viral infections may produce a myocarditis

*Hypertensive and Arteriosclerotic Heart Disease* —The cardiac disability resulting from hypertension and arteriosclerosis of the coronary arteries comprise more than 50 per cent of all heart disease While either of these factors may be the dominant or perhaps the sole cause of the heart disease they are commonly associated to a varying extent These two types of cardiac disability are occasionally observed in patients past forty years and are largely responsible for the high mortality rate from heart disease after fifty years of age

*Syphilitic Heart Disease* —This is one of the more serious forms of cardiovascular disease The course, after the onset of the symptoms is usually progressively downward Cardiovascular disability due to syphilis is occasionally observed between the ages of twenty and thirty years but is seen more often between the ages of forty and fifty five years

*Thyrotoxic Heart Disease* —The cardiac disability associated with toxic adenoma and exophthalmic goiter constitutes an important form of heart disease in certain sections The incidence is greatest in the Great Lakes region and the Pacific Northwest and relatively low in certain of the eastern and southern states This form of cardiac disease is most common between the ages of thirty and forty five years Within recent years a form of cardiac disability has been ascribed to myxedema

*Congenital Heart Disease* —The various congenital anomalies of the heart and great vessels comprise only a small percentage of the total incidence of cardiac disease Many of the minor forms are not recognized during life and are of importance only in so far as they may contribute to the development of a cardiac infection

*Conditions Contributing to a Cardiac Disability* —Chronic pulmonary disease such as bronchitis fibrosis and emphysema promotes the disability of an already damaged heart and upper respiratory infections not infrequently precipitate cardiac failure Deformities of the chest and spine particularly kyphoscoliosis by producing a displacement and possibly a compression of the great vessels as well as by seriously curtailing the peripheral vascular bed of the lungs may impose a serious handicap on the heart Obesity increases the work of the heart and perhaps favors the development of arteriosclerosis High grade anemia especially of the pernicious type occasionally unmasks a latent cardiac disability the cardiac symptoms may in fact, be the first to attract the attention of the patient Excessive physical exertion very often promotes the onset of cardiac failure after sixty years of age Pregnancy is another factor which may contribute to an existing impairment in the cardiac function especially if mitral stenosis is the antecedent lesion

## METHODS OF EXAMINATION

The taking of a proper case *history* is probably the most important part of a cardiac examination As a matter of fact in the diagnosis of coronary artery disease especially in its early stages the history may establish the diagnosis even when all the usual studies are negative This is best illustrated by angina pectoris of which the diagnosis is dependent entirely on the history

*Physical examination* is the next most important step in arriving at a diagnosis In most cases inspection palpation and auscultation of the patient will make the diagnosis apparent The physical examination for heart disease is the same as any other physical examination except for this—that special positions may be helpful in eliciting murmurs and thrills

*Roentgen study* may be divided into several categories at the present time By fluoroscopy of the patient in the right and left anterior-oblique views as well as in the posterior-anterior view one may study the size of the heart chambers the heart contours the pulmonary artery vascular lung markings diaphragmatic excursions and aortic size and pulsations The teleoroentgenogram (taken at a distance of 6 feet or 1 8 meters) is most valuable for determining heart size

*Roentgenkymography* has been shown to be valuable in studies of pericardial disease, aneurysm of the left ventricle, and time relationships of chamber activities

*Cinematography* offers an excellent means of studying the heart in action This method records the fluoroscopic image of the heart on motion picture film for later study *Tomography*, though not often used in the study of heart disease, may be valuable in distinguishing mediastinal masses from the heart as well as in the study of aneurysms

More recently *angiocardiography* both in single and double plane, has been used With this method the actual size of the heart chamber as well as that of the heart wall may be determined Abnormal shunts and narrowed valve orifices may also be found this way *Aortography* is useful for determining the site and length of aortic coarctation, aortic width and length, and the presence of patent ductus The two methods just mentioned, since they involve the use of diodrast in 70 per cent concentration for delineation, have certain dangers for the cyanotic patient

The *electrocardiograph* is a very helpful instrument in cardiologic diagnosis However, one must remember that it is meant to be only an aid, like any other laboratory test and is not the *sine qua non* that many people believe it to be At present one should take, as a minimum, the three standard leads as well as six precordial leads At times, high precordial leads or precordial leads to the right of the sternum may also be necessary before one finds definitive changes Unipolar limb leads may be helpful in determining the electrical position of the heart as well as the significance of a Q3 in the electrocardiogram One may use with uniform success either string or amplifier-type instruments either direct writers or those equipped with photographic paper *Vectorcardiography*, which records the mean electrical forces active in the heart at any given moment promises to be important in the future of electrocardiography

At times one may wish to use is part of an office procedure either *anoxemia* tests or *exercise* tests with the electrocardiograph to elicit coronary insufficiency In these tests the presence of insufficiency is determined by depression of the S-T segments or flattening or inversion of the T-waves immediately after the exercise or during the period of anoxia *Exercise tests using pulse rate and blood pressure determinations* have also been used to measure heart reserve The pulse rate and blood pressure must return to the resting levels at the end of two minutes to be considered normal *Venous pressure determinations* may be most helpful in determining early heart failure The normal venous pressure is from 40 to 100 mm water *Circulation times* may help differentiate dyspnea of pulmonary origin from that of cardiac background The normal circulation times are as follows arm to lung time—4 to 8 seconds (ether) arm to tongue time —10 to 16 seconds (decholin calcium gluconate) These times are prolonged in congestive heart failure polycythemia vera and myxedema They are shortened in hyperthyroidism anemia beriberi heart disease, arteriovenous fistula certain types of congenital heart disease, and febrile states

*Vital capacity* is also used as a test of cardiac reserve The patient exhales as much as possible into a spirometer after inhaling as deeply as possible Reduction in vital capacity may indicate early heart failure

*The stethocardiograph* records heart sounds With it the examiner can both determine the exact timing of the sounds and study their pattern and frequency The *oscillometer* is a most useful office instrument for it helps confirm or deny the pulse findings in cases of peripheral vascular disease

*The ballistocardiogram*, once a most cumbersome instrument for the recording of cardiac thrust' has now been simplified so remarkably that it has become an office instrument With it one may record data which cannot be determined by any other means With a standardized instrument one is able to measure cardiac output It is useful in diagnosing masked hyperthyroidism, coarctation of the aorta early coronary artery disease and the anginal syndrome

*Cardiac catheterization* to record chamber pressures as well as to remove blood samples for oxygen determination promises to be one of our most useful procedures in the

study of heart disease A radioopaque catheter is passed through the antecubital vein into the brachial vein then the axillary vein and then the superior vena cava From here it is passed into the right auricle the right ventricle and the pulmonary artery In the presence of septal defects the catheter may be passed into the chambers on the left side of the heart These studies are particularly valuable in cases of congenital heart disease and rheumatic heart disease and in investigations of renal vascular physiology and various phases of hemodynamics Intracardiac electrocardiography can also be done through this catheter

## MANIFESTATIONS OF HEART DISEASE

The most important symptoms of heart disease are the following

*Dyspnea* —Shortness of breath on exertion is one of the earliest and most frequent manifestations of heart disease The exact mechanism is not established but it is apparently related to reduced vital capacity This symptom is only of importance when compared to the normal response to a given exercise by a given individual all other etiologic causes excluded Certain people have a limited tolerance to exertion normally In the early stages of heart failure the patient notices that he becomes winded on exertion that previously has not caused discomfort Later he finds that less exercise is required to induce the shortness of breath Frequently at this time edema begins to appear in the ankles and if the impairment in the cardiac function progresses the dyspnea becomes more evident and even exists during rest in the upright position—orthopnea Under these circumstances the mere change to a recumbent position may produce intense shortness of breath This change in posture further reduces the already limited vital capacity Usually by this time there is extensive edema with marked congestion of the lungs engorgement of the liver and possibly fluid in the pleural and peritoneal cavities This constitutes the advanced stage of congestive failure

*Paroxysmal Dyspnea —Cardiac Asthma —Acute Left Heart Failure* —In the cardiac disability resulting from hypertension arteriosclerosis of the coronary arteries and coronary occlusion syphilitic aortitis and disease of the aortic valves the dominant effect is on the left ventricle The syndrome of left heart failure is also observed in mitral stenosis and rapid ectopic rhythms This syndrome may finally terminate in insufficiency of the left ventricle before there is a corresponding reduction in the functional capacity of the right ventricle thus resulting in pulmonary congestion and hence a reduction in vital capacity With further suppression of the function of the left ventricle without corresponding effect on the right ventricle but with resulting increase in pulmonary congestion paroxysmal dyspnea occurs The attacks are precipitated by factors that increase the demands on the heart Attacks may occur during the day after exertion or excitement later in the course of the cardiac disability they frequently occur at night and awaken the patient from a sound sleep The dyspnea is commonly preceded or accompanied by a hacking cough and frequently a tight sensation or a feeling of heaviness in the chest These attacks are usually aborted by the patient s assuming an upright position With the progression of the cardiac disability the subject may be awakened many times during the night and finally reaches the stage when he is no longer able to sleep in a recombent position because of the frequent recurrence of the respiratory distress Acute left ventricular failure is one of the important syndromes of the hypertensive arteriosclerotic and syphilitic forms of heart disease Pulmonary congestion is a prominent feature in high grade mitral stenosis and with exertion or paroxysmal tachycardia paroxysmal dyspnea may occur

*Acute Pulmonary Edema* —This results from an advanced state of pulmonary congestion Thus a severe attack of paroxysmal dyspnea (acute left ventricular failure) may progress to acute pulmonary edema It is manifested by an intense air hunger coughing extreme cyanosis or perhaps more often an ashen gray color profuse cold perspiration the raising of copious frothy blood tinged sputum and the pres-

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ence of numerous moist râles throughout the chest. The prognosis is grave and if recovery occurs there is always a possibility of a recurrence.

*Cheyne-Stokes Breathing.*—This form of breathing is commonly observed in advanced cardiac failure of arteriosclerotic origin, particularly that associated with a hypertension, and is of *grave prognostic significance*. It also occurs in uremia and diseases of the central nervous system, especially with *acute increase of the intracranial pressure*. There are various grades of this condition. The earliest stage consists of a periodic increase and diminution in the depth of respiration. Periodic breathing of this general type is often noted during sleep in infants and elderly subjects, may follow the administration of hypnotics, such as morphine and chloral, and is common in high altitudes. That referred to in the present discussion is characterized by alternating periods of apnea and hyperpnea occurring in regular sequence. In the beginning, it appears only during sleep but in advanced stages *it may last for many hours or days*. During the period of apnea, which may last from twenty to thirty seconds, the patient becomes drowsy and often falls asleep. With the subsequent onset of breathing the respiration gradually becomes more labored and when fully established, the subject is aroused or awakened with a start at the height of the hyperpnea. The hyperpnea then subsides in the same manner in which it appeared and sleep is again resumed with the return of the apnea. Various explanations have been advanced for this condition and there is still diversity of opinion concerning the underlying mechanism of this syndrome.

*Precordial and Substernal Pain.*—Substernal or precordial discomfort ranging in degree from a feeling of fullness or heaviness to the agonizing and terrifying pain which occurs in certain instances of angina pectoris and coronary occlusion, is a common complaint in cardiac disease. The pain of angina pectoris and coronary occlusion is the most distinctive of all cardiac symptoms. In the former, the distress is invariably precipitated by anything which increases the work of the heart, more particularly exercise and excitement. It is generally first felt somewhere under the sternum, usually over the upper or lower regions and frequently involves the precordium. It may later extend to the left shoulder and down the left arm, and in the more severe form *may be felt in both arms*. *In certain instances*, the pain is transmitted to the neck and head. The distribution varies considerably *in different individuals*. In some, the pain or paresthesia, may appear first at a peripheral point, as in the wrist, arm, neck or head, and later be felt in the chest; in others, the pain may be confined to the lower sternum and epigastrium, or even entirely to the upper abdomen. The distress in its mild form consists of a substernal feeling of fullness or heaviness or of constriction. It is often first noticed while climbing a hill or going up stairs or during excitement, and promptly disappears after the exercise is discontinued or the excitement subsides. Later, the distress is more easily precipitated, is of a more severe character, and is possibly transmitted to the various regions mentioned. The pain of coronary occlusion *is of a similar character but often more* severe, possibly has a wider range of distribution, and may persist in a minor form even after repeated injections of morphine. It is likely to occur while at rest and very often awakens the patient from a sound sleep. This pain is frequently most intense over the lower sternal region and may likewise be confined almost entirely to the epigastrium.

*Precordial distress* often assumes other forms. It may be dull and more or less continuous or transient, sharp and stabbing in character. It is frequently a prominent feature of acute rheumatic heart disease, particularly when there is involvement of the pericardium. It is occasionally observed in chronic valvular heart disease, especially mitral stenosis and aortic insufficiency; frequently occurs with abnormal cardiac mechanisms such as premature contractions, paroxysmal tachycardia, auricular fibrillation and auricular flutter; may result from the toxic influence of tobacco and is one of the outstanding symptoms of the effort syndrome. In such cases a hypersensitive state of the nervous system is often an important factor. If there is doubt concerning implica-

tion of the heart the possibility of intercostal neuralgia nerve root involvement from a destructive lesion in the spine hypertrophic osteoarthritis or a mediastinal tumor should be considered

*Palpitation* —This symptom is usually not of great importance as an indication of a significant impairment of the cardiac function It is however frequently the first to direct attention to the heart and often causes great concern on the part of the patient Its occurrence after violent exertion or intense and sudden excitement represents a normal physiologic reaction It is frequently associated with premature contractions paroxysmal tachycardia auricular fibrillation and auricular flutter Consciousness of the heart is a common symptom in thyrotoxicosis a prominent feature of the effort syndrome and may be one of the early complaints in pulmonary tuberculosis It is not infrequently observed during convalescence from various infections during the menopause and in high grade anemias Other factors as abdominal flatulence fatigue coffee alcohol and tobacco may induce or aggravate palpitation Since this symptom may be associated with such a variety of extracardiac conditions a careful history and a detailed examination are necessary in order to determine its significance

*Other Signs and Symptoms* —Many of the symptoms of heart disease are produced by secondary disturbances in the function of such organs as the lungs gastro-intestinal tract and brain

A *cough* usually indicates pulmonary congestion and may be a prominent feature in cases in which the cardiac failure develops during acute or chronic bronchitis in cardiac asthma acute pulmonary edema and aortic aneurysm The sputum is ordinarily scanty except in chronic bronchitis or in pulmonary edema In the latter the expectoration of a large amount of frothy blood tinged sputum is one of the characteristic symptoms Slight hemoptysis is frequently seen in congestive heart failure and is seen especially in mitral stenosis occasionally frank hemorrhage occurs Hemoptysis in association with cough may indicate an acute pulmonary embolism *Abdominal discomfort* which is not referable to angina pectoris or coronary occlusion is often a conspicuous feature of early cardiac failure A feeling of fullness or heaviness and the consciousness of gas after meals are usually the first of these symptoms to appear They are followed by soreness in the right upper quadrant caused by engorgement of the liver and in some instances by anorexia and even nausea and vomiting The digestive disturbance is due to deranged gastric function consequent upon passive congestion but it is frequently mistaken for a sign of digitalis intoxication When the hepatic congestion develops rapidly the distress caused by distention of the capsule may be severe enough to simulate an acute surgical condition The pain in pericarditis may be referred to the upper abdomen by way of the phrenic nerves

*Cerebral manifestations* such as headaches dizziness and faintness are common in arteriosclerotic heart disease and are not infrequently observed in association with aortic stenosis or insufficiency various types of abnormal cardiac mechanism and in the effort syndrome The Adams-Stokes syndrome is occasionally encountered This syndrome includes dizziness faintness syncope and possibly convulsions It is usually accompanied by cardiac standstill a very slow ventricular rate a rapid ventricular tachycardia or ventricular fibrillation Psychosis sometimes develops during the course of cardiac failure and may be very disturbing An occlusion of a cerebral vessel sometimes occurs from an embolus originating in the heart

*Insomnia* may occur as a manifestation of early congestive heart failure Insomnia may be secondary to cerebral anoxia but is more often the result of paroxysmal nocturnal dyspnea unrecognized by the patient as such

*Fatigability* may be one of the earliest and most prominent symptoms and often progresses to a feeling of exhaustion A loss of 10 to 20 pounds in weight is not uncommon in more prolonged and advanced forms of congestive failure

*Cyanosis* or blueness of the lips and nail beds may be a symptom of heart disease This is usually present when the peripheral blood contains 5 grams of hemoglobin in the

reduced state Ordinarily, this is seen in cases of chronic congestive failure, acute congestive failure and certain types of congenital heart disease This cyanosis must be distinguished from cyanosis due to stasis and cyanosis due to primary pulmonary disease or other cause (*See* Chapter 22)

*Edema* —With right sided heart failure swelling of the ankles will occur This occurs first at the end of the day when the patient has been on his feet for some time This may disappear during the night when the patient is recumbent only to recur at the end of the next day If not treated the edema will involve the legs and finally may be found over the entire lower half of the body These findings will be accompanied by liver enlargement and one may even find ascites at times If the patient is recumbent for any period of time the edema will be found over the sacrum since this is the most dependent portion of the body in this position This edema must be differentiated from the edema seen in kidney disease and that resulting from such local causes as varicose veins or from hypoproteinemia Cardiac edema is pitting in type as opposed to the swelling seen in myxedema

*Pallor* may be a symptom of heart disease secondary to anemia such anemia as accompanies rheumatic heart disease or subacute bacterial endocarditis or the pallor may be the result of shock as in acute coronary occlusion or may be seen in advanced arteriosclerosis

*Jaundice* may also occur when there is considerable blood destruction as in subacute bacterial endocarditis or pulmonary infarction, and in association with liver congestion in congestive heart failure

*Precordial Bulging* usually indicates a rheumatic mitral heart lesion, one acquired before the patient's seventh or eighth year Such bulging however may occasionally be due to an interauricular septal defect

*Venous Distention* is found both in the vessels of the neck and in the vessels of the arms in cases of heart failure One may measure the height of venous pressure roughly by noting at what point above the heart level the veins in the arms collapse Pericarditis may also produce venous distention in the neck, especially in cases of so called upper mediastinal syndrome

*Pulsations* —Abnormal pulsations in the chest will be noted when the heart is hypertrophied, especially in the thin chested and in patients with aortic or tricuspid insufficiency In cases of adherent pericardium there is often systolic retraction of the sternal wall and other portions of the precordial area In cases of coarctation of the aorta there is pulsation of the intercostal and the scapular vessels

*Heart Enlargement* is a common result of all heart disease Sometimes it is reversible as in myxedema heart and beriberi, usually, however, the condition is progressive

*Cardiac Murmurs and Thrills* may be functional or organic in origin, sometimes it is difficult to distinguish between them These thrills and murmurs will be discussed later as will arrhythmias of the heart which may constitute important evidence of cardiac abnormality

*Liver Enlargement* is a common result of right heart failure It must be differentiated of course from cirrhosis of the liver and enlargement of the liver due to other disease or to metastatic invasion of the liver The liver in heart disease however is usually tender with the edge smooth It usually decreases in size with adequate therapy Pericarditis is a common cause of liver enlargement and must always be considered when an enlarged liver is found

*Ascites* is often an important sign of heart failure but may be due to liver disease or metastatic involvement of the peritoneum In ascites due to heart failure there is moderate or marked leg edema

*Rales* —Rales at the base of the lungs are characteristic of left heart failure They should not be confused with bronchitis or bronchiectasis The râles of heart failure are often difficult to differentiate from those of pneumonitis which are often associated with heart failure

*Eye Grounds* —In hypertensive heart disease the changes in the eye grounds are frequently of help in determining the severity of the condition As the disease progresses, one may see the narrowing and loss of the normal contour of the retinal arteries

and the development of hemorrhages and retinitis

## RHEUMATIC HEART DISEASE

Rheumatic heart disease includes the cardiac involvement associated with or following the various manifestations of rheumatic fever and that which is represented at a later stage by disease of the myocardium valves and pericardium even though the history of an etiologic factor is often lacking (For detailed discussion of these points *see* Chapter 18)

## BACTERIAL ENDOCARDITIS

When pathogenic bacteria enter the blood stream and are carried to all parts of the body they start localized inflammatory processes more readily in some places than others One of the commonest of these sites is the endocardium of the valve leaflets and the disease which is produced in this way is known as bacterial endocarditis It may be initiated by many different kinds of bacteria The disease manifests itself as an endovascular infection characterized chiefly by embolic phenomena Two forms the acute and subacute are ordinarily recognized They differ not only in their clinical course but also from an etiologic standpoint in that the acute form is generally secondary to some other disease as pneumonia puerperal sepsis furunculosis gonorrhea whereas in the subacute form the bacterial portal of entry is usually unknown

Acute Bacterial Endocarditis —*Etiology* —Previously acquired or congenital disease of the endocardium seems to predispose it to attack Various organisms have been described but the Streptococcus hemolyticus the pneumococcus Staphylococcus aureus and the gonococcus are the causative agents in the vast majority of cases

*Morbid Anatomy* —The infection of the endocardium leads to tissue destruction and the formation of vegetations In some of the more severe forms there may be extensive destruction of the valve and even ulceration of the adjacent myocardium The vegetations are grayish cauliflower like masses of varying size made up of fibrin platelets leukocytes red blood cells and bacteria The infection may invade any part of the endocardium or the chordæ tendineæ or even the intima of the aorta but is most commonly observed on the valves particularly those of the left heart and about congenital defects The pathologic changes outside the heart aside from those of the primary condition (*e g* pneumonia furunculosis) consist of various types of vascular lesions many of which are embolic in origin These lesions are essentially perivascular hemorrhages about the terminal vessels They ordinarily occur on the skin and mucous membrane as petechiæ and are observed on the serous surface of the internal organs in sizes varying from that of a pin head to large areas such as are produced by occlusion of splenic or renal arteries Cerebral hemorrhage is one of the common pathologic findings in this disease

*Signs and Symptoms* —The symptoms in the beginning may be overshadowed by those of the primary condition (pneumonia puerperal sepsis) and the onset of the acute bacterial endocarditis not recognized but in many cases the onset of the disease is clearly defined The patient who has perhaps not appeared seriously ill is suddenly taken with chills and fever The symptoms in general are those of sepsis with chills and profuse sweating at irregular intervals high fever marked prostration and often delirium The discovery of a murmur or the knowledge of preexisting heart disease may focus attention on the heart The spleen is perhaps enlarged and may be tender The leukocyte count ranges from 10 000 to 30 000 Sooner or later petechiæ are observed on the skin or conjunctivæ The urine frequently shows a trace of albumin and often red blood cells The causative organism may be isolated from the blood stream The disease is not infrequently complicated by occlusion of large vessels in the spleen kidneys brain extremities and possibly mesentery It often pursues an unfavorable course and may terminate in death within a few days or weeks As a matter of fact if the disease lasts over two months it is arbitrarily called subacute bacterial endocarditis even though it fits the other criteria of acute bacterial endocarditis

There may be rupture of the papillary muscle as a result of this condition When this occurs, there may develop acute left-heart failure with rapid, persistent pulmonary congestion There may also be heard a loud, whistling "to and fro murmur at the apex

*Diagnosis* — The first physical sign to appear is *an endocardial murmur, or perhaps* a change in the character of a preexisting murmur, when this occurs in the course of *severe systemic infection it suggests endocarditis* Embolic phenomena and recovery of the bacteria from the blood complete the diagnosis

*Treatment* — *Until recently the disease* was uniformly fatal Penicillin and streptomycin, however have reduced this death rate The treatment consists in giving the patient about 1 000,000 units of penicillin daily This treatment is continued for four weeks, then the patient is observed for a few weeks Recently other of the newer antibiotics have also been used with good results By sensitivity tests, one can determine the best antibiotic to use in each case Under certain circumstances, one may even *find a combination more effective than any* one of the antibiotics

Cures have been obtained in about 60 per cent of the cases

Subacute Bacterial Endocarditis — Subacute bacterial endocarditis is a more common disease than the acute form but is nevertheless comparatively rare In a series of heart cases reported by White and Jones, its general incidence was 1–2 per cent and its incidence in the rheumatic group 4 per cent

*Etiology* — The Streptococcus viridans is the etiologic agent in 90 to 95 per cent of all cases *Although various other organisms* may cause the disease, the influenza bacillus and the gonococcus are the most important causative agents in the remaining 5 to 10 per cent

The onset of subacute bacterial endocarditis has often been traced to a tooth extraction or tonsillectomy or infection of the upper respiratory tract all three are often associated with a transient bacteremia Involvement of the endocardium is apparently facilitated by previous valvular disease or by a congenital anomaly Chronic valvular (aortic and mitral) heart disease precedes subacute bacterial endocarditis in a large percentage of cases The mitral valve seems to be more often affected in cases with simple mitral insufficiency than in those with tight mitral stenosis Subacute bacterial endocarditis may become engrafted upon an active rheumatic infection In these cases it is believed that the bacteria invade the thrombin platelets on the valve edges and there become implanted and grow *in a protected medium The principal pre*disposing congenital defect is a bicuspid aortic valve or patent ductus arteriosus The highest incidence *falls between the ages of twenty and thirty years* the disease is seldom encountered after fifty years In the older patients, atheromatous or syphilitic changes occasionally furnish the predisposing factors

*Morbid Anatomy* — Here again infection of the endocardium produces destructive lesions which may be very extensive In the more chronic form, less destruction occurs and various stages of healing may be encountered The vegetations vary greatly in extent, appearance and consistency *They may be confined to a small section of* a valve leaflet but are usually more extensive involving possibly the chordae tendineae the walls of the ventricles or auricles or even the aorta They are usually small, nodular, with perhaps short pedunculated clumps but not infrequently occur in the form of large irregular masses club shaped or strap like projections The large pedunculated formations are usually quite firm in consistency, often present fibrous tissue formation and occasionally calcareous deposits showing the tendency of the disease to heal Certain *of the vegetations are so friable* that they are easily broken off and carried out into the circulation These lesions usually occur in the left heart, involving either the mitral or aortic valves possibly more often the latter, but both may be affected In rare instances the infection may begin on the tricuspid or pulmonary valves When emboli appear in both the pulmonary and general circulation it usually means that the *vegetations are clustered* about a defect in the interventricular septum Minute perivascular hemorrhages occur in the skin, mu

cous membranes and the serous surfaces of the internal organs and large infarcts in various organs particularly the kidneys spleen and brain In the kidney partial thrombosis of the glomeruli produces a characteristic type of nephritis (focal glomerulonephritis)

In the myocardium in cases of subacute bacterial endocarditis two types of lesions have been described—the Aschoff nodule and a granuloma caused by calcific deposits the result of calcific emboli arising from healing vegetations of the aortic valve This latter lesion is found only in cases in which the subacute bacterial endocarditis has been treated with either sulfonamide compounds or penicillin

The lesions found in the heart at autopsy in cases in which the patients though cured of subacute bacterial endocarditis died of a complication (heart failure pulmonary embolus cerebral hemorrhage or embolus uremia) are similar to those found in the cases of spontaneous healing only the lesions in the former are more complete and uniform All the vegetations have disappeared leaving shrunken valves with flat scarred and calcified plaques In some cases even though clinical cure has been established (negative blood cultures) very small fibrous tags or elevations covered by fibrin may be found These tags consist of bacteria fibrin and platelets situated on the denuded endocardial surface The base of the lesion shows various degrees of organization and fibrous tissue formation Some calcification and at times new capillary formation are also noted Some cases also show large areas of fibrosis such as would be seen after an acute myocarditis These cases apparently are those most likely to go into heart failure since there is also marked damage to the valve In some of these healed cases not only may the valve be invaded through the fibrin meshes on top of the involved endocardium it may also be attacked by direct infiltration through the capillaries

*Symptoms* —The onset is usually insidious and the symptoms in the beginning are often very indefinite The patient may note that he tires easily and possibly has aches and pains in various parts of his body He may relate his illness to some recent infection particularly of the upper respiratory tract While the patient may be aware of an old cardiac lesion he seldom connects his disability with the heart In time a daily fever is discovered and perhaps chilly sensations are experienced The onset is occasionally more abrupt with chilly sensations or even a frank chill and fever Fever is usually present to a variable extent throughout the course of the disease although there may be afebrile periods for days or even weeks In mild cases the temperature rises from perhaps 99° F in the morning to 100 or 101° F in the evening with an occasional ascent to 102° F In severe cases high fever of a remittent type is the rule The general symptoms of systemic infection fatigability, anorexia loss in weight and possibly joint pains continue as the only manifestations of the disease until the embolic phenomena make their appearance

Symptoms from emboli vary with the organ involved and the size of the vessel occluded Hemiplegia may occur from the occlusion of a cerebral vessel pain may occur in the left upper quadrant of the abdomen and the lower left chest from a splenic infarct and intense pain may occur in the leg and be followed by gangrene as a result of the blocking of a femoral artery Occasionally a mesenteric vessel is occluded giving rise to very severe abdominal pain shock nausea and vomiting constipation or diarrhea with perhaps bloody stools and possibly later the signs of intestinal obstruction Any of the above major embolic accidents may occur early in the course of the disease

In some cases pain in the back may be caused by renal embolization

*Objective Signs* —Pallor is common and when combined with the yellow faint brown or muddy tint to the skin ( cafe au lait color) may be the first feature to attract the attention of the examiner The signs in the heart are generally those of a chronic valvular lesion of the mitral valve the aortic valve or both In rare instances the history and signs suggest one of the congenital anomalies such as a defect in the interventricular septum or persistent ductus arterio

sus The spleen is usually enlarged and palpable Embolism gives rise to a variety of signs Gross infarction of the spleen or kidney, occlusion of the femoral artery or hemiplegia from cerebral embolism may be among the earliest manifestations of the disease In other cases there is at first nothing to suggest subacute bacterial endocarditis except the symptoms of infection, a valvular lesion or the history of heart disease and an enlarged spleen, but diligent search is rewarded sooner or later by the discovery of petechiae These tiny hemorrhagic spots appear periodically in the skin retina and mucous membranes, perhaps most characteristically in the conjunctivae and pass slowly through the usual color changes before they disappear Occasionally the hemorrhages are so large that they may properly be called ecchymoses The appearance of tender areas in the pulp of the fingers and toes is a closely allied phenomenon These areas are bluish red in color quite tender and occasionally palpable They usually disappear within a few hours or days Clubbing of the fingers not infrequently develops during the course of the disease

Some patients have, as an early symptom areas of transient phlebitis with ecchymosis

Secondary anemia develops as the disease progresses and in some cases becomes a prominent feature A hemoglobin of 40 to 60 per cent and a red cell count of 2,500 000 or 3 500 000 are common The hemoglobin may however recede to 30 or even 20 per cent and the red cells to 1,500 000 The leukocytes vary in number They generally range between 12 000 and 18 000 and occasionally increase to 25 000 In many instances there is no significant leukocytosis The blood cultures usually show Streptococcus viridans but it may be necessary to make repeated cultures using large amounts of blood before a positive result is obtained If antibiotics have been used before the blood culture is taken the culture medium must be so prepared as to inactivate the antibiotic and permit the infecting organism to grow A culture must be given an adequate time for growth before it is decided that the culture is negative Furthermore if the clinical picture is that of subacute bacterial endocarditis, it is advisable to take new cultures if the first are negative

The urine usually shows a trace of albumin, hyaline and granular casts and frequently red blood cells The kidneys may be damaged extensively either by occlusion of the large renal vessels or as a result of multiple thrombosis of the glomeruli Occlusion of the capillary loops by small emboli produces a characteristic type of nephritis which occasionally progresses to renal insufficiency

*Diagnosis* —The clinical course of subacute bacterial endocarditis, aside from the embolic manifestations, is not unlike that of any protracted infection In the preembolic stage it may be confused with various other infectious diseases, such as pulmonary tuberculosis typhoid fever, malaria and undulant fever Typhoid and undulant fever are generally eliminated by the agglutination test And in undulant fever, the sedimentation rate is normal Subacute bacterial endocarditis should be considered and blood cultures made in any patient with a heart lesion and an obscure fever The conjunctiva, mucous membrane of the mouth and pharynx, skin and eye grounds should be examined daily for petechiæ In all cases the blood culture is the most important diagnostic measure and should be repeated until the diagnosis is established Subacute bacterial endocarditis may occasionally be confused with active rheumatic heart disease, but the embolic phenomena and positive blood cultures complete the differentiation

*Prognosis* —If the disease is untreated death usually results from exhaustion intercurrent infection (*e g* pneumonia) cardiac failure or the occlusion of a large vessel particularly of the brain or the lung In some cases renal insufficiency is an important terminal factor

If the disease is treated with penicillin the recovery rate is about 80 per cent Streptomycin and some of the newer antibiotics may raise the recovery rate still higher In general the younger the patient the better the chance of recovery Oddly enough patients with congenital heart disease show the highest recovery rate

When the patient has recovered from subacute bacterial endocarditis as the result of treatment there are other factors which may alter his prognosis Heart failure may occur any time after the patient has recovered from the acute infection This was the most common cause of death after recovery The reason for this is understood when one looks back at the pathology after recovery from the infection Cerebral hemorrhage also seems to play a role as a cause of death possibly due to damage of the cerebral vessel from the preexisting disease Coronary thrombosis may also occur Uremia though not common is also one of the possible causes of death as the result of kidney damage occurring before the institution of treatment

After recovery from subacute bacterial endocarditis relapse or reinfection is also possible Seventy five per cent of the cases that relapse do so within 30 days after treatment has been stopped Others however may not relapse for from 3 to 7 months Recurrence of the original infection or infection with a different organism may occur at any time In either case treatment may be instituted as will be outlined below, just as if the patient had never been treated before

*Treatment* —In subacute bacterial endocarditis the patient should be kept on an adequate diet with an adequate intake of fluids His metabolic requirements should be regularly checked upon so that he does not develop any nutritional deficiency Before antibiotics are used the offending organism must be isolated and its sensitivity to the antibiotics tested Penicillin is usually the therapeutic agent of choice especially against streptococcus viridans Streptomycin is used against Gram negative or penicillin resistant organisms The use in subacute bacterial endocarditis of aureomycin chloromycetin and terramycin is so new that they cannot yet be properly evaluated The sulfonamides and the anticoagulants have pretty generally been discarded in the treatment of subacute bacterial endocarditis In the treatment of the disease there is no unanimity of opinion on what the daily dosage of penicillin should be how long the therapy should last or what the best method of administration is In general however it seems advisable to maintain a blood level 5 or 10 times the minimal amount effective *in vitro* One may achieve these high levels of penicillin in the blood stream not only by using large doses of the drug but also by using kidney blocking agents such as caronamide Generally speaking one uses between 1 000 000 and 2 000 000 units of penicillin daily In the treatment of relapses a substantial increase in both the daily dose and the duration of treatment should be made regardless of the sensitivity of the organism The usual length of treatment for the original infection is from 4 to 6 weeks The patient s clinical response regulates his dosage if there is no improvement the amount of antibiotic should be increased Occasional embolic phenomena early in the course of treatment are to be expected and are not to be construed as indicative of therapeutic failure

In cases in which streptomycin is used it is advisable to give the patient at least 3 grams of it daily by intermittent intramuscular injection In certain cases it is necessary to combine penicillin with streptomycin for best results It is always reasonable to begin treatment with penicillin no matter what the *in vitro* sensitivity tests show for often the *in vivo* response is much better than the *in vitro* test would indicate If large doses of penicillin fail it is advisable to use streptomycin If this too is ineffective other antibiotics as well as the sulfonamides may be used

In addition to the antibiotic therapy it is advisable to keep the patient s sodium intake low since congestive heart failure is often a complication Transfusions are usually unnecessary but should be used without hesitation if one is faced with a dangerously low or falling hemoglobin value during therapy Digitalis is indicated only if congestive failure develops Oral iron preparations will combat the secondary anemia and high potency multiple vitamin mixtures may be desirable for supportive care It is not necessary to confine the patients to bed during the entire course of therapy If the patient is strong enough to get out of bed and shows no evidences of congestive heart

failure it is probably advisable to keep him out of bed

After treatment has been discontinued, it is advisable to take weekly blood cultures for four weeks The patient should of course be carefully supervised from this point on for the rest of his life in order to detect any reinfection

*In cases of patent ductus arteriosus* it has been shown that cure can be achieved very rapidly by ligating the patent ductus, this despite the fact that the patient has subacute bacterial endarteritis The use of penicillin preoperatively and postoperatively helps sterilize the blood stream and clear up the disease Some cases have been cured by surgery alone

*Prophylaxis* —In view of what has been said under etiology and pathogenesis it is obvious that patients with rheumatic or congenital heart disease should be protected against subacute bacterial endocarditis Adequate prophylaxis should be employed before tooth extractions or operations on the nose the throat the ears or the genitourinary tract Penicillin should be given in doses of 300 000 units daily intramuscularly 24 hours before such procedures and for 2 or 3 days after In this way, the bacteremia will be adequately controlled and the likelihood of infection of the endocardium diminished

## HYPERTENSIVE CARDIOVASCULAR DISEASE

(see Chapter 24)

## CORONARY-ARTERY DISEASE (ANGINA PECTORIS AND CORONARY OCCLUSION)

Coronary-artery disease is essentially arteriosclerosis of the coronary vessels (See Chapter 24 for discussion of arteriosclerosis)

*Etiology* —The cause of the disease is unknown There are, however a number of factors thought to contribute to the development of the disease Of these, the following are the most important (1) *Heredity* (coronary artery disease runs in families and is associated particularly with hypertension and diabetes, the latter accelerates the arteriosclerotic process by five to ten years), (2) *temperament* (reactions to situations both external and internal are believed to play a great role in the development of coronary-artery disease), (3) *infection* (streptococcic infections typhoid fever, rheumatic fever, and syphilis often contribute to the development of the disease), (4) *obesity* (coronary artery disease is more common in the overweight) (5) *smoking* (patients under 40 who develop the anginal syndrome or coronary thrombosis show a high proportion of heavy smokers—*i e*, those who smoke 30 or 40 cigarettes or a proportional number of cigars a day) (6) *physical effort* (excessive or prolonged physical effort may cause coronary insufficiency and myocardial infarction), (7) *nervous tension* (if prolonged for hours may induce coronary artery disease) (8) *occupation* (if routine is strenuous physically or mentally coronary artery disease may develop), (9) *sex* (coronary-artery disease principally affects men in women it is chiefly associated with hypertension or diabetes) and (10) *age* (coronary artery disease occurs chiefly in persons between 50 and 70)

*Pathology* —In addition to arteriosclerosis, the pathology of coronary artery disease embraces myocardial infarction or death of the heart muscle Though it may sound paradoxical, myocardial infarction may be found without coronary occlusion and in some cases coronary occlusion may be found without myocardial infarction Infarction of the heart without occlusion occurs in patients who have coronary artery disease and suffer diminution of blood flow through shock as the result of peritonitis vomiting cerebral accident operation etc It may also occur when the patient with narrowed coronary arteries engages in effort so great as to cause a relative anoxia Coronary occlusion without myocardial infarction occurs when a coronary vessel narrows so gradually that the heart muscle can adjust itself to the altered cardiovascular dynamics Furthermore the patient may die so soon after an occlusion of the coronary vessel takes place that infarction cannot develop In such cases the vessel contains a fragile,

friable small reddish thrombus, easily missed because organization of the clot has not had time to take place

With the occlusion of small arterial twigs there may be only small areas of fibrosis in the myocardium areas which may be detected only by histologic examination whereas with occlusion of a larger artery there may be extensive necrosis and fibrosis In the occlusion of a large artery the extent of the damage depends on the degree of anastomosis and on whether the occlusion is sudden or gradual If the vessel is gradually occluded and the neighboring artery which contributes to the blood supply of the involved section of the cardiac musculature is not involved conditions are most favorable for the further development of the collateral circulation Under these circumstances more and more of the arterial supply involved is taken over by the neighboring vessels and the complete occlusion of the first even though terminated abruptly may be followed by surprisingly satisfactory recovery the possibility of infarction may not even be suspected during the patient s life

With extensive necrosis the left ventricular wall occasionally ruptures permitting hemorrhage into the pericardial sac and causing death There are other instances in which the destructive process is so wide spread that a section of the wall of the left ventricle is largely replaced with fibrous tissue Bulging of this area of the ventricular wall may result and form an aneurysm This usually involves the anterolateral apical region of the left ventricle after the occlusion of the anterior descending branch of the left coronary artery

The changes in the cardiac musculature predominate in the left ventricle In general there are three types of lesions The first is represented by the small area of fibrosis resulting from the closure of the small arterial twigs these are detected only by histologic examination The second is manifested by a more extensively localized area of degeneration and replacement with fibrous tissue The most characteristic lesion of this type is produced by the occlusion of the anterior descending branch of the left coronary artery It involves the anterior apical wall of the left ventricle the lower anterior section of the interventricular septum and to a varying extent the adjoining anterior wall of the right ventricle There is a striking variation in the extent of the lesion depending on the degree of the collateral circulation The third type of lesion is that of disseminated degeneration and fibrosis of the endocardial and subendocardial layers of the lateral and posterior walls of the left ventricle it frequently involves a portion of the posterior section of the intraventricular septum This lesion is seen in its most typical form following the occlusion of the circumflex branch of the left coronary artery and to a lesser extent following the closure of the terminal descending branches of this vessel or the corresponding branches of the right coronary artery

Damage to the papillary muscles of the mitral valve is an important feature in the occlusion of the coronary arteries The papillary muscles are likely to be involved by the occlusion of either of the main branches of the left coronary artery The changes in these structures contribute to the alteration in the first heart sound at the apex and to the production of the systolic murmur frequently heard in this location Sclerotic changes of the coronary vessels frequently occur in association with aortic stenosis

*Pathologic Physiology* —Coronary blood flow varies with the demands on the heart It is increased by exercise emotion increased metabolic rate and rapid ectopic rhythms The coronary flow is slight during systole and maximal during diastole Therefore the length of the diastolic period is very important in determining the coronary blood flow The flow through these vessels is decreased by narrowing of the lumen of the coronary arteries by disease vasospasm (if this occurs in the coronary arteries) and certain drugs such as pituitrin

It is felt by many that vagus stimulation decreases coronary blood flow whereas sympathetic stimulation increases coronary blood flow As can be readily seen these nerves and their action will be under reflex control and will be altered by emotional strain reflexes from the gastrointestinal tract the bladder and the brain and

reactions to various drugs and stimulants There are also chemical controls of coronary circulation Anoxia, lactic acid, and other products of fatigue, as well as changes in the acid base balance, produce coronary dilatation

Though many of these mechanisms of control are still subject to much discussion and have not been entirely proved, it might be wise, at this point, to define three terms which are often used in discussion of coronary artery disease The first of these is *coronary insufficiency* This term is much abused and denotes different things to different people Perhaps it is best not to use it at all, since some people use it synonymously with coronary-artery disease, which it certainly is not Actually, coronary insufficiency means that there is a discrepancy between the need for blood flow to the heart and the available blood supply It signifies merely an inadequate coronary flow at a particular time In the normal heart one can exceed the available supply by inordinate demands in the absence of any coronary vascular disease The term *coronary failure* has recently come into use and should be briefly discussed In this state, the patient experiences an attack of substernal pain and/or pressure, which may last for from 15 minutes to 2 hours The electrocardiogram may show little or no changes, in spite of the length of time of the attack Such a patient is considered to have an impending coronary occlusion and should be treated with bed rest and anticoagulants, as will be discussed later under the treatment of coronary occlusion, in order to try to prevent an occlusion or thrombosis and myocardial infarction Another term to be defined is *anginal syndrome* * The range between the level of basal coronary blood flow and that at which the patient develops symptoms is narrower in patients with the anginal syndrome than in the normal This results in the characteristic symptoms of substernal pain or, in some cases of substitution symptoms such as dyspnea pains in the arms or back pulmonary edema and *syncopal* attacks In the anginal syndrome in addition to the characteristic substernal pressure which demands that the patient stop his effort immediately there are certain characteristic electrocardiographic changes demonstrable during the attack These consist of ST-segment deviation, which will return to the base line as soon as the attack is over

This being clearly understood, one may go on to discuss some of the causes of coronary insufficiency This state may be produced by decreased blood flow, as in shock, aortic insufficiency, and coronary sclerosis Or there may be a qualitative deficiency of the blood flowing in the coronary arteries, that is there may be a decreased oxygen content in the blood as in anemia and anoxic states Further there may be increased work on the part of the heart without an equivalent increase in coronary blood flow, and, finally, in hypertrophy of the heart one may see coronary insufficiency One must remember that homeostatic mechanisms tend to compensate for certain qualitative changes, in anemia for example the velocity of the blood flow is increased and the viscosity decreased and this tends to make up for the lack of oxygen-carrying capacity of the blood

The typical anginal syndrome is usually caused by (*a*) excessive exertion (*b*) excessive emotional strain (*c*) excessive food intake (*d*) tachycardia (*e*) vasomotor reflexes (*f*) positional changes, (*g*) hypoglycemia (*h*) high altitudes, (*i*) states leading to hemorrhage shock, anoxemia, and asphyxia (*j*) certain drugs (ephedrine) (*k*) asthma

In patients with coronary failure or angina pectoris or even in those without symptoms certain factors may precipitate a coronary occlusion *Exertion* is a common precipitating factor This may produce true coronary failure or as a result of the effort there may be a rupture of an arteriosclerotic plaque blocking the involved coronary artery *Mental strain* will also affect the coronary circulation and lead to occlusion *Lowering* of the *blood pressure* as a result of *shock anesthesia* or *syncope* will slow up coronary circulation and so lead to thrombosis *Digestive disturbances* may produce coronary insufficiency as the result of increasing the work of the heart as well as by reflex effects upon the coronary circulation *Arrhythmias* will increase the work of the heart and, at the same time, reduce diastolic filling of the coronary arteries thereby

* The anginal syndrome is due to an insufficient amount of coronary blood flow resulting from an increased demand made upon the heart at a given time

precipitating coronary failure and thrombosis. Diarrhea and vomiting will dehydrate the patient and lead to electrolyte imbalance and shock. Thus the production of coronary thrombosis and infarction may result. *Trauma* may injure a coronary vessel and lead to occlusion.

*Symptoms.*—The symptoms of coronary-artery disease depend on the previous state of the heart, the amount of coronary involvement, and the nervous make-up of the patient. The preeminent symptom in coronary-artery disease is pain. Its location is important. Substernal pain is more significant than precordial pain. It is usually pressing, constricting, and vise-like rather than sharp, lancinating, or stabbing. Furthermore, it usually occurs upon effort and excitement and occasionally after meals. The combination of exertion after eating will usually precipitate an attack in any patient with this condition. (A *meal* increases the work of the heart by as much as 50 per cent.) The pain may radiate to the left arm, to the left side of the back, neck, and shoulder, to both shoulders, or to both arms, or extend to the neck and chin. In the anginal syndrome, the pain lasts about five minutes and not over fifteen and usually disappears upon resting; in myocardial infarction the pain is severe and lasts from two hours to several days and is not relieved by rest. Occasionally it may be accompanied by shock. In the intermediate group the pain lasts from fifteen minutes to two hours without electrocardiographic changes. This may indicate the presence of a precoronary occlusion state (so-called coronary failure) or it may be a myocardial infarction in a "silent area" of the heart. These attacks continue until a major occlusion or a myocardial infarction occurs. It is important to recognize this intermediate group in order to keep the patient in bed for two or three weeks and so postpone the development of a major catastrophe.

With the onset of the pain there may also be some shortness of breath. If the attack is a severe one, there may also be sweating and collapse. The patient with the anginal syndrome usually stops whatever he is doing and remains in a frozen immobile state. The patient with myocardial infarction, on the other hand, will very often be restless and walk around in an effort to "walk off the pain" and to overcome the feeling of angor animi. Aerophagia and belching are frequent concomitants of the attack.

*Signs.*—The signs will depend on the previous state of the heart and the severity of the coronary artery disease. In patients with angina pectoris there will be no signs during the attack. However, when coronary occlusion or myocardial infarction occurs, then the signs will be readily found. The patient will usually appear to be ashen gray and pallid. There may or may not be some cyanosis of the lips and nailbeds. There is usually profuse sweating, and the patient will usually be dyspneic. The blood pressure will often fall, though in a certain percentage of cases there will be a marked rise in blood pressure during the acute attack. The heart will often be enlarged to percussion. (This is present in ⅔ of the cases and is usually due to preexisting hypertension or long-standing coronary-artery disease with gradual heart enlargement.) Heart sounds will be of poor tonal quality. There may or may not be a gallop rhythm. The pulse will be soft and easily compressible. A systolic murmur may be heard at the apex. This murmur will usually start late in systole and is due to atrophy of the posterior papillary muscle. Arrhythmias may appear, *e.g.*, sinoauricular or auriculo-ventricular heart block. The development of auricular fibrillation is usually indicative of infarction of the auricular muscle. Ventricular tachycardia is a dangerous type of ectopic rhythm and is usually found when the infarction is extensive and involves a large portion of the interventricular septum. Pulsus alternans, mechanical or electrical, is frequently present but usually transient. This is indicative of severe myocardial damage. Left heart failure when seen during the acute stage of myocardial infarction is a bad prognostic omen. (The mortality rate may be 50 per cent when acute pulmonary edema accompanies myocardial infarction.) Rectal temperature may be elevated or normal, though it is usually above normal. However, this

rise in temperature will usually not occur during the acute stage but will develop within 12 to 24 hours. And then there will also be a leukocytosis and an increase in the erythrocyte-sedimentation rate. About 36 to 48 hours after the onset of the infarction one may hear a pericardial friction rub in a certain number of cases. This is usually heard when there has been an anterior myocardial infarction though lateral and rarely posterior infarctions may produce a friction rub, since the epicardial inflammation may extend well beyond the actual area of infarction.

*X-ray Findings.*—The x-rays of patients with angina pectoris will usually show little if any deviation from the normal, although on fluoroscopy, there may be diminution in the amplitude of cardiac pulsation. In cases of long-standing coronary-artery disease there may be evidences of left-ventricular hypertrophy. In patients with acute myocardial infarction one may see on fluoroscopy areas of paradoxical pulsation indicating the point at which there has been an infarction. But fluoroscopy should not be done if the diagnosis is established. The x-ray may show some cardiac enlargement if there has been preexisting disease before the myocardial infarction. During the acute stage there may also be an increase in hilar markings indicative of early left ventricular failure. There may also be evidences of sclerosis of the aorta with calcification. In some rare cases calcification of the coronary vessels may also be seen. After recovering from the acute attack, the patient may develop aneurysm or dilatation of the left ventricle. Roentgen studies will demonstrate this.

*Electrocardiographic Findings.*—The electrocardiograms of coronary artery disease vary from normal tracings to those typical of myocardial infarction. In the early stages of coronary artery disease one may find no changes in the electrocardiogram. In the presence of angina pectoris one may see ST-segment deviations during the actual attack of angina. However, these will rapidly return to normal. In advanced stages of coronary artery disease one may find inverted T waves in various leads as well as slurring of the QRS complexes with no evidences of acute myocardial infarction. In addition there may be evidences of bundle-branch block or auriculo-ventricular nodal delay with varying degrees of heart block. Other arrhythmias may occur as a result of coronary artery disease.

In the presence of acute myocardial infarction certain characteristic changes will occur. However, it is essential to remember that one cannot make a diagnosis of myocardial infarction on the electrocardiogram alone. Many cases of myocardial infarction will show no electrocardiographic changes for several days after the infarct, so that serial tracings are most important. Also in some few cases, the presence of the myocardial infarction cannot be picked up by the electrocardiograph at all. When changes are present in the electrocardiogram, however, they are of great help in diagnosis.

*In acute myocardial infarction* there are usually two characteristic types of curves. The first of these is usually associated with myocardial infarction of the so-called anterior type, the other with myocardial infarction of the so-called posterior type. Anterior infarction so-called is usually associated with disease of the left coronary artery and posterior infarction with that of the right coronary artery. But variations in the anatomy of these vessels may confuse the picture. In anterior myocardial infarction the ST segment is elevated in Lead I and in left precordial leads and depressed in Lead III. In time the ST segments return to the base line and are replaced by sharply inverted T waves in Lead I and in the precordial leads and an upright deflection of the T waves in Lead III. It must be remembered, however, that in some cases the ST segment may not be elevated or its elevation may be so transient that it is not picked up by the electrocardiograph. In addition, in anterior myocardial infarction a Q wave or a prominent initial negative deflection will occur in Lead I as well as in the precordial leads. The position in the precordial leads in which the Q wave is found depends on what area of the anterior myocardium is involved. Usually the changes are seen somewhere between the $V_2$ and $V_6$ positions of the precordial leads. In posterior myocardial infarction there will

be a depression of the ST segment in Lead I, and in the precordial leads, with an elevation in Lead III, followed by a return to the base line and then a negative T wave in Lead III with a positive T wave in Lead I and high voltage T waves in the precordial leads The Q wave will now be seen in the third lead instead of in the first lead These patterns have been called Q 1 T 1 for the anterior infarction and Q 3 T-3 for the posterior infarction The augmented unipolar limb leads are particularly helpful in the diagnosis of posterior and lateral wall infarctions aVF will show Q waves of significant depth and/or width, and inverted T waves in cases of posterior infarction In lateral wall infarctions aVL will show significant Q waves, S-T segment changes and T-wave inversions At times esophageal leads may be necessary for the diagnosis of posterior myocardial infarction The electrocardiogram is continually changing in the early stages of myocardial infarction this is important to diagnosis It is imperative to take electrocardiograms at one- or two-day intervals or oftener to make the diagnosis In time the T wave changes may revert to normal though in most cases they never become upright again However the Q wave will persist for most of the rest of the patient's life Additional electrocardiographic *tracings of so-called antero-lateral* and lateral wall infarctions as well as postero lateral patterns have also been described Furthermore one may see what is now called the high antero-lateral type of myocardial infarction These will all give patterns which vary somewhat from those which have been described However in spite of the fact that they are not exactly like those that have been described they follow similar changes and therefore are readily recognized if enough leads are taken in the proper positions

*Diagnosis* —The diagnosis of coronary artery disease can be made upon the symptoms and signs as outlined as well as upon the electrocardiographic and roentgenographic findings But it is often important to resort to some of the more specialized tests for coronary insufficiency None of these tests are ideal and using them is fraught with a certain amount of danger since they may precipitate an attack of myocardial infarction or an arrhythmia which may result in death Therefore they must be used with great caution and only after careful thought Those most commonly used are one of several types of exercise test such as the Master two-step test, and the anoxemia test In the latter, the patient is given a mixture of 10 per cent oxygen and 90 per cent nitrogen to breathe and changes in the electrocardiogram are noted

*Differential Diagnosis* —In the differential diagnosis of coronary artery disease there are many conditions which must be considered One must first of all consider disease of the chest wall and musculature as well as of the spine and the nerves leading from it Therefore one must rule out arthritis of the spine neuritis myositis, etc Diseases of the gastrointestinal tract may also be confusing, especially in the differential diagnosis of myocardial infarction Here one must consider such things as gall bladder disease, perforating peptic ulcer and pancreatitis Disease of the mediastinum must also be considered in the differential diagnosis Pulmonary embolism and pleurisy may also be confusing in some cases There are, in addition a group of cardiovascular diseases other than coronary-artery *disease which may also give chest* pain These include aortic disease valvular disease of the heart such as aortic stenosis, and insufficiency as well as mitral valvular disease pericarditis arterial hypertension syphilis of the aorta rheumatic heart disease thyroid heart disease congenital heart disease, dissecting aneurysm of the aorta rupture of the aorta into the pericardial sac and acute pneumothorax However by careful history *x* ray examination and the use of the electrocardiogram, one may usually make the proper diagnosis without great difficulty Of course there will always be certain cases which are most confusing and which will only be diagnosed after careful and prolonged study

*Complications* —The complications of coronary occlusion are many Arrhythmias occur frequently immediately after the occlusion and may be fatal Shock and acute left heart failure occur so often with

myocardial infarction that they are often considered part of the disease rather than complications Chronic left-heart failure may develop after the acute phase is over This may last for many years and eventually lead to death Right heart failure may result from the left-heart failure and may further complicate the picture

Emboli are also a common complication of this condition They may come from mural thrombi formed at the site of infarction on the endocardial surface or may come from the leg veins as a result of venous stasis from prolonged bed rest Pulmonary emboli from the leg veins are the most common type found at autopsy Cerebral emboli are also a most serious form of complication Visceral emboli usually strike the spleen or kidney but may also involve the alimentary tract Peripheral emboli may also occur Saddle emboli of the bifurcation of the aorta are the most serious of this type though there may be emboli found at the bifurcation of any of the peripheral vessels

Rupture of the heart is not an uncommon cause of death in the first two weeks after a myocardial infarction It may occur in the first few days but ruptures have been reported as late as the seventeenth day after an infarction (the peak incidence is on the ninth day) The factors responsible for the rupture are softening of the cardiac musculature and the height of the intraventricular pressure Activity of the patient seems to play a role in precipitating this complication, and it may be the cause of many of the so-called ' bedpan deaths ' in which the strain of moving the bowels raises intraventricular pressure and causes a blowout of the myocardium When there is rupture one sees a hemopericardium, cardiac tamponade, and sudden death Usually, it takes about 250 cc to 1000 cc of blood to produce tamponade If the leak of blood is slow there may develop an electrocardiographic pattern of a pericarditis engrafted upon that of the myocardial infarction Usually, death occurs in from a few minutes to an hour so that often no clinical diagnosis can be made

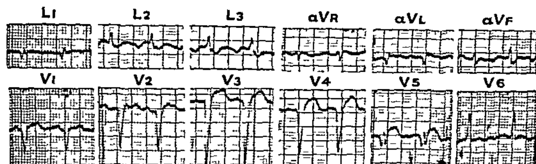



Fig 138 —*Acute Anterior Myocardial Infarction* —Note Q wave in lead 1 and aVL Note absence of R wave in V1 2 3 4 and 5 Note elevation of RT segments particularly marked in V3 4 and 5

Rupture of the interventricular septum is a rare complication of myocardial infarction When it occurs, it is single and is found in the lower or central portion of the septum The patient becomes suddenly dyspneic and shows signs of increasing shock Right-sided heart failure develops rapidly and a loud systolic murmur and thrill are found in the fourth and fifth interspace near the left sternal border The survival time is from a few months to five years The patients manifest persistent right- and left heart failure

Rupture of a papillary muscle as the result of myocardial infarction is a rare complication The posterior papillary muscle of the left ventricle is most often affected In such cases one hears a loud apical systolic murmur or a whistling to and fro murmur or a murmur and thrill like that heard in rupture of the interventricular septum This is usually accompanied by left heart failure

Aneurysm of the left ventricle occurs as a result of intraventricular tension which stretches the noncontracting infarcted area of the heart It may bulge very little and

then only in systole or the aneurysm may be large enough to simulate a tumor. It is usually seen months after the infarction, though it may develop quite early. There are usually no symptoms from this condition. On physical examination it may present a pulsation separable from the apex beat. The $x$ ray may reveal an outpouching on the left ventricular contour, especially in the oblique positions. Fluoroscopy and roentgenkymography may reveal a paradoxical pulsation in the left ventricle at the aneurysmal site. The electrocardiogram will often show an elevation in the precordial leads of the ST segments as evidence of an aneurysm.

Sudden death is a common complication of myocardial infarction. The causes of the sudden death are the infarction, massive pulmonary embolism, ventricular rupture, ventricular fibrillation, cardiac standstill due to vagal reflexes following ventricular tachycardia, Stokes-Adams syndrome with complete heart block and cardiac standstill. The intravenous use of certain drugs, such as aminophyllin, papaverine and quinidine, may also cause sudden death. A second *infarction of the myocardium may also* occur and cause death. This may result from a retrograde extension of the original thrombosis or may be due to the development of a second thrombus in another vessel.

The so-called "shoulder hand" syndrome is also a complication of coronary occlusion. In this condition one finds a stiffness of the shoulder joint with pain in this region and limitation of motion of the shoulder joint, shoulder girdle and arm. This may attack the right or left shoulder but is more common on the left, producing a so-called "frozen shoulder." It usually develops about four weeks after the occlusion and may last six months to two years with spontaneous cure. But it may recur. The hand and wrist may also be involved, giving pain, stiffness and swelling of finger joints and changes in the palm suggesting early Dupuytren's contracture. The cause of this complication is not known but is believed to be a causalgic type of disturbance mediated through sympathetic reflexes secondary to pain stimuli.

*Prognosis.*—Prognosis in coronary artery disease is most difficult to evaluate. In cases of angina pectoris, for example, though sudden death is always a possibility, recovery may occur without cardiac changes. Some patients with angina pectoris have been known to live for many years. The outlook is determined to a certain extent by the condition of the cardiovascular system. Frequent and severe attacks of course always make the outlook gloomy. In a patient with syphilitic aortic insufficiency the development of the anginal syndrome usually indicates a rapid downhill course. The prognosis in general is most favorable when it is not possible to demonstrate significant structural changes in the heart and the attacks are mild and infrequent. The angina associated with arrhythmias and high grade anemias may frequently be eliminated by the treatment of these conditions. The general temperament of the patient is also important. In the very high strung, little organic change will produce more marked symptoms than in the phlegmatic, and this may confuse the prognosis. Finally, patients careful in complying with the recommendations of their physicians *may add years to their lives. To disregard* factors which excite the pain may precipitate death.

Prognosis in myocardial infarction is also a difficult problem. The immediate prognosis is always grave; about 25 per cent of those stricken with the disease die during the first attack. Death from myocardial infarction usually occurs within the first 5 days of the condition and is usually rather sudden. Death is also common, however, during the first two weeks after infarction; here death follows cardiac rupture or a complication like a pulmonary or cerebral embolism. Patients who survive this period may die as a result of progressive cardiac failure or have another infarction later. It has been shown that 25 per cent of all cases of myocardial infarction survive 10 years, 18 per cent survive over 10 years, and 50 per cent survive 5 years or more. In general the course of the condition is most favorable when the heart withstands the occlusion without signs of heart failure and grave when extensive impairment of cardiac function occurs during the initial stages of the occlusion. But there are numerous exceptions.

The course is also dependent to a remarkable extent on whether treatment is given immediately after the occlusion. Even though the heart damage may not seem great the chances of recovery may be lessened if the patient is permitted to get on his feet again too soon.

Within the next few years prognosis in myocardial infarction may be much better than it is today for anticoagulants which may help prevent some of the complications are being developed and widely used.

*Treatment.—Anginal Syndrome.*—In the treatment of this condition, it is imperative, first of all, to treat the patient's general mental condition properly. He should be reassured and told how to avoid extraneous tensions likely to strain the heart. The drug of choice in the treatment of this condition is nitroglycerine. This is given in doses of from 0.3 to 0.6 mgm. in hypodermic tablets. One tablet is placed under the tongue at the onset of an attack. In addition to being used for acute attacks nitroglycerine may be used prophylactically; the patient may take a nitroglycerine tablet before he engages in an effort which he knows will bring on an attack of angina pectoris. In addition some have recommedned the use of doses of 0.15 mgm. of nitroglycerine every 2 hours as a means of preventing anginal attacks. Other vasodilators, such as amylnitrite (one pearl by inhalation), sodium nitrite (0.06 Gm. three times daily), erythrol tetranitrate (0.015 to 0.03 Gm. three times daily) and mannitol hexanitrate (0.015 to 0.03 Gm. three times daily) have also been used for the treatment of the anginal syndrome. Alcohol has also been highly recommended since it is one of the best vasodilators available but it is important to remember that after two or three drinks, some persons develop a false sense of physical prowess which may be harmful rather than helpful. Further alcohol dilates peripheral vessels and so increases the work of the heart. The xanthine drugs have also been used in the treatment of the anginal syndrome but their exact value in preventing attacks is not clear. Injecting alcohol in the posterior roots of the ganglia from C 8 to D-4 has also been used when the attacks are severe and frequent. This treatment, however, may cause such complications as pneumothorax and neuritis. Some investigators have recommended that the patient's basal metabolic rate be lowered. Such agents as propylthiouracil and radioactive iodine are used to accomplish this. The great disadvantage is that they often cause myxedema, with all its attendant complications.

*Myocardial Infarction.—Treatment.*—It is imperative during the attack of acute myocardial infarction to relieve the pain, for the pain aggravates the shock, increases the work of the heart and causes reflex constriction of the unaffected coronary vessels. For this the drug of choice is morphine sulfate in doses of 0.010 to 0.12 Gm. This is usually given subcutaneously; however, in many cases, it is better to give it from 10 to 15 mgm. intravenously. It is also considered advisable to give atropine sulfate in doses of from 0.6 to 1.2 mgm. with the morphine because atropine neutralizes the vagus effect responsible for the constriction of the coronary arteries. Papaverine in doses of from 0.06 to 0.2 Gm. given intravenously, also acts as a coronary dilator. It must be given slowly. This drug has the disadvantage of causing transient attacks of ventricular fibrillation and also increases the work of the heart. Aminophyllin has been given intravenously but should not be used; it increases the work of the heart out of proportion to its vasodilating effect.

Next to morphine oxygen is probably the most valuable agent in the treatment of myocardial infarction. It relieves both the pain and the anoxia and may be given either by mask or by tent. Quinidine sulfate may be given if extrasystoles either auricular or ventricular or paroxysmal auricular tachycardia develops with the infarction. The dose is from 0.3 to 0.6 Gm. taken orally every hour. It may be necessary to use the intramuscular route if shock exists. Some workers now use this drug prophylactically since it not only prevents arrhythmias but may also be effective as a coronary dilator. Procaine amide 250 mgm. to 1 gram every 4 hours has been found to be particularly effective in ventricular tachycardia and extrasystoles. It is also effective in paroxysmal auricular tachycardia but not in estab

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The diet for patients with myocardial infarction should be low in calories to reduce demands on the heart Bed rest for from 4 to 6 weeks is desirable The patient should not however be frozen in bed but should be advised to use his arms and legs early in the attack though not to engage in any strenuous effort Straining on the bedpan is particularly dangerous because this type of strain produces a Valsalva experiment with damaging effect upon the coronary circulation and through this upon the heart The result is sudden death (so-called bedpan death)

At present the acute attack is also being treated with such anticoagulants as heparin and dicumarol The theory behind this is that such agents will prevent (*a*) the retrograde spread of a thrombus (*b*) the development of phlebothrombosis and hence the formation of pulmonary and other emboli The patient's daily coagulation time and prothrombin time determine how and in what dosage these anticoagulants are to be used With heparin the coagulation time is prolonged to 30 minutes for adequate results The prothrombin time is kept at three times the control level with Dicumarol for its best effect One favored routine is to give 50 mgm of heparin intravenously and 300 mgm of Dicumarol by mouth at once Fifty mgm of heparin is given intramuscularly every 4 hours thereafter for 48 hours or until effective levels are reached with Dicumarol Protamin will counteract the effect of heparin and vitamin K and blood will correct excess Dicumarol with bleeding Daily urine tests are used to detect early bleeding

If shock occurs both blood and plasma transfusions have been recommended But the exact status of this therapy for myocardial infarction shock is not yet certain

*Between Attacks* —How to treat a patient after an attack of acute myocardial infarction depends on the case It is of course important to teach him how to live and to restrict his activities in order to prevent extra strain on his heart And every such patient should rest every afternoon to reduce the work done during the day and divide the strain of work Smoking should be discouraged Whether drugs other than sedatives should be used to keep the patient in a relaxed frame of mind is a most important question There are those who believe in the use of xanthines others use papaverine in large doses orally as a prophylactic and as a means of keeping the coronary circulation at its best 0 09 to 0 2 gm four times daily) Alcohol has also been highly recommended Recently Khellin or Visammin in doses of 40 to 50 mgm four times daily has been recommended as a coronary dilator Its value is still debatable

Though various surgical operations have been devised to increase the circulation to the myocardium none have proved of great value In one type of operation the omentum is brought up and attached to the heart In another talc is injected in the pericardial sac to form adhesions More recently Claude Beck has anastomosed the aorta to the coronary sinus by means of a vein graft The end of the sinus nearest its point of emptying into the right auricle is then partially occluded This causes a reversal of the blood flow to the myocardium The efficacy of this operation in patients with coronary artery disease awaits further evaluation

## CARDIOVASCULAR SYPHILIS

*Incidence* —(*See* Chapter 3 )

*Pathology* —Syphilis shows a predilection for the root of the aorta but it often involves the entire ascending portion less frequently the arch and occasionally the descending aorta In rare instances the lesion may be confined to the abdominal aorta If the aortic valve area and the orifices of the coronary arteries are spared by the syphilitic process the heart is not likely to be damaged The early lesion consists of an endarteritis obliterans of the vasa vasorum and a perivascular infiltration of lymphocytes in the media This is associated with degenerative changes in the media and results in the destruction of the elastic structures and a weakening of the vessel wall The process finally extends to the intima and the aortic

The course is also dependent to a remarkable extent on whether treatment is given immediately after the occlusion. Even though the heart damage may not seem great, the chances of recovery may be lessened if the patient is permitted to get on his feet again too soon.

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The course is also dependent to a remarkable extent on whether treatment is given immediately after the occlusion. Even though the heart damage may not seem great, the chances of recovery may be lessened if the patient is permitted to get on his feet again too soon.

Within the next few years, prognosis in myocardial infarction may be much better than it is today, for anticoagulants which may help prevent some of the complications are being developed and widely used.

*Treatment.—Anginal Syndrome.*—In the treatment of this condition, it is imperative, first of all, to treat the patient's general mental condition properly. He should be reassured and told how to avoid extraneous tensions likely to strain the heart. The drug of choice in the treatment of this condition is nitroglycerine. This is given in doses of from 0.3 to 0.6 mgm. in hypodermic tablets. One tablet is placed under the tongue at the onset of an attack. In addition to being used for acute attacks, nitroglycerine may be used prophylactically; the patient may take a nitroglycerine tablet before he engages in an effort which he knows will bring on an attack of angina pectoris. In addition, some have recommedned the use of doses of 0.15 mgm. of nitroglycerine every 2 hours as a means of preventing anginal attacks. Other vasodilators such as amylnitrite (one pearl by inhalation), sodium nitrite (0.06 Gm. three times daily), erythrol tetranitrate (0.015 to 0.03 Gm. three times daily) and mannitol hexanitrate (0.015 to 0.03 Gm. three times daily) have also been used for the treatment of the anginal syndrome. Alcohol has also been highly recommended since it is one of the best vasodilators available, but it is important to remember that after two or three drinks some persons develop a false sense of physical prowess which may be harmful rather than helpful. Further, alcohol dilates peripheral vessels and so increases the work of the heart. The xanthine drugs have also been used in the treatment of the anginal syndrome but their exact value in preventing attacks is not clear. Injecting alcohol in the posterior roots of the ganglia from C-8 to D-4 has also been used when the attacks are severe and frequent. This treatment, however, may cause such complications as pneumothorax and neuritis. Some investigators have recommended that the patient's basal metabolic rate be lowered. Such agents as propylthiouracil and radioactive iodine are used to accomplish this. The great disadvantage is that they often cause myxedema, with all its attendant complications.

*Myocardial Infarction.—Treatment.*—It is imperative during the attack of acute myocardial infarction to relieve the pain, for the pain aggravates the shock, increases the work of the heart and causes reflex constriction of the unaffected coronary vessels. For this the drug of choice is morphine sulfate in doses of 0.010 to 0.12 Gm. This is usually given subcutaneously; however, in many cases, it is better to give it from 10 to 15 mgm. intravenously. It is also considered advisable to give atropine sulfate in doses of from 0.6 to 1.2 mgm. with the morphine because atropine neutralizes the vagus effect responsible for the constriction of the coronary arteries. Papaverine in doses of from 0.06 to 0.2 Gm. given intravenously, also acts as a coronary dilator. It must be given slowly. This drug has the disadvantage of causing transient attacks of ventricular fibrillation and also increases the work of the heart. Aminophyllin has been given intravenously but should not be used; it increases the work of the heart out of proportion to its vasodilating effect.

Next to morphine, oxygen is probably the most valuable agent in the treatment of myocardial infarction. It relieves both the pain and the anoxia and may be given either by mask or by tent. Quinidine sulfate may be given if extrasystoles, either auricular or ventricular, or paroxysmal auricular tachycardia develops with the infarction. The dose is from 0.3 to 0.6 Gm. taken orally every hour. It may be necessary to use the intramuscular route if shock exists. Some workers now use this drug prophylactically since it not only prevents arrhythmias but may also be effective as a coronary dilator. Procaine amide 250 mgm. to 1 gram every 4 hours has been found to be particularly effective in ventricular tachycardia and extrasystoles. It is also effective in paroxysmal auricular tachycardia but not in estab-

tients with syphilis or with a positive Wassermann the following evidence is suggestive of aortitis A loud systolic murmur in the second right intercostal space a tambour like second aortic sound associated with normal blood pressure, and localized bulging of the ascending aorta In a few cases a serrated appearance of the first portion of the ascending aorta and increased diameter of the first portion of the ascending aorta (as measured by angiocardiography) are present In the absence of arteriosclerosis a width of over 38 millimeters for the first portion of the ascending aorta is indicative of syphilitic aortitis Occasionally there is pulsation in the first or second left intercostal space or in the suprasternal notch The presence of T wave inversions or other signs of coronary insufficiency with signs of syphilis in the absence of arteriosclerosis indicate syphilitic aortitis

In syphilitic aortic insufficiency the Wassermann is positive in about 95 per cent of the cases particularly if treatment is inadequate If signs of aortic regurgitation are present and the Wassermann is negative the chances are against syphilis as the cause of the valvular lesion The typical auscultatory and peripheral signs of aortic regurgitation are usually present In some cases of syphilitic aortic insufficiency, a diastolic rumble may be heard at the mitral area (Austin Flint murmur) The Austin Flint murmur is observed chiefly in cases of syphilitic aortic regurgitation and only rarely in cases of rheumatic aortic disease

The signs of an aortic aneurysm may not be present if the aneurysm is small and located in the sinus of Valsalva If large it gives a characteristic x ray and fluoroscopic picture Aneurysm of the ascending aorta may produce pulsations in the second intercostal space to the right of the sternum The ascending aorta is anterior to the main right stem bronchus Hence an aneurysm in this location does not produce pressure on the latter In aneurysm of the transverse arch pulsations are seen in the suprasternal notch They are due to transmission from and the dilatation of the innominate artery and not to transmission from the aorta itself We may also get brassy cough unequal pulses and blood pressures tracheal tug and pupillary signs Aneurysm of the descending aorta frequently produces pain because of the erosion of the vertebrae It also causes pressure against the main left stem bronchus with obstruction and atelectasis of the left lung The heart is small or normal in size unless the aneurysm is complicated by another syphilitic lesion Abdominal aneurysm occurs much less frequently than thoracic aneurysm The ratio is about one to ten The symptoms in the abdominal type occur late The pain is usually due to erosion of the spine The aneurysm causes pressure and may rupture into the abdomen On abdominal palpation, one may find a painful expansile pulsating tumor in the abdomen particularly in the epigastrium The blood pressure in the legs will be lower than the blood pressure in the arms X ray will disclose erosion of the vertebrae and perhaps calcification of the aneurysmal sac One may be able to outline the aneurysmal sac by injecting a radio-opaque dye into the femoral artery or into the aorta under pressure

*Differential Diagnosis* —In the presence of a systolic aortic murmur and a loud tambour like second aortic sound hypertensive heart disease must be ruled out In the presence of hypertension the diagnosis of coëxistent syphilitic aortitis is difficult to make

In considering the differential diagnosis of aortic insufficiency, rheumatic heart disease becomes of primary importance A patient between 20 and 30 with a history of rheumatic fever a mitral lesion left auricular enlargement and possibly auricular fibrillation probably has rheumatic heart disease and not syphilis A patient between 35 and 45 with a history of chancre a positive Wassermann and no mitral lesion *probably has syphilis and not rheumatic heart disease*

A diminished cardiac reserve without obvious cause in a patient with positive serology or heart failure in a syphilitic patient below forty without valvular lesion will usually indicate syphilitic aortitis In the differential diagnosis of aortic aneurysm the age group is important as is the fact that from 45 to 55 per cent of abdomina

valve structures, producing in the typical case varying degrees of wrinkling and puckering of the former with intervening areas of depression and a thickening and shortening of the valve leaflets In some instances the valve leaflets may be so extensively deformed that they are reduced to fibrous bands A widening of the commissures is one of the earliest and most distinctive manifestations of an involvement of the aortic valve area

The scarring of the aorta leads to a contraction which may result in narrowing of the lumina of the great vessels leaving the aorta The most important site of narrowing is in the region of the coronary ostia The site of narrowing becomes the seat of atheromatous deposits and a secondary thrombus formation This accounts for differences in blood pressure and pulse in symmetrical portions of the body in the absence of aneurysm Distally the coronary arteries are normal, only the ostia being implicated The effect is to produce coronary insufficiency However, this occurs slowly allowing the heart to develop collateral channels and to adapt itself so that its compensation is maintained Circulatory insufficiency from such narrowing of the openings of the branches coming off the aorta may be widespread It may involve the intercostal arteries and cause severe back pain due to *ischemia*

The syphilitic aortic valvulitis which results in thickening and deformity of the leaflets or a separation of the commissures will result in aortic regurgitation Scarring may also extend down and involve the left branch of the bundle of His This gives rise to a left bundle branch block Though the amount of regurgitation and the resultant cardiac strain may vary the prognosis is fairly good when there is no involvement of the coronary ostia for the heart is then better able to adjust itself to the greater load In this case the patient may attain the age of 60 to 65 But in the type of aortic regurgitation associated with narrowing of the coronary ostia and in which the nutrition of the heart muscle is already impaired the presence of aortic regurgitation results in the early production of congestive failure

Aneurysm of the aorta frequently occurs as the result of syphilis Aneurysm, single or multiple may also occur in any portion of the arch the abdominal aorta, or the peripheral vessels Such aneurysms often cause pressure on adjacent structures as bone esophagus, bronchi, etc and occasionally rupture Aneurysm of the pulmonary artery is rare Some cases of Ayerza's disease are thought to be due to syphilitic involvement of the pulmonary artery branches Gumma of the heart is rare Syphilitic myocarditis as originally described by Warthin, is also rare Instances of syphilitic infiltration of the myocardium have been observed in cases of malignant syphilis

*Symptoms* —Dyspnea and pain are the outstanding symptoms of syphilitic aortitis and each generally indicates an extensive impairment of the cardiac function The dyspnea is usually the first expression of congestive failure and in time is followed by congestion of the lungs, engorgement of the liver and edema of the extremities In the beginning it is either manifested by shortness of breath on slight exertion or occurs in the form of paroxysmal dyspnea Paroxysmal dyspnea is not infrequently the first symptom It may occur at any time possibly precipitated by exertion but often appears during the night Pain may be a very prominent symptom and may or may not be associated with dyspnea It varies in character from an ill-defined distress over the precordium or a sense of constriction or burning over the upper sternum to the typical pain of angina pectoris The pain may be constant, often comes in attacks and may be initiated by exertion It may be confined to a relatively small area or transmitted to the neck shoulders or arms In some cases the pain is presumably aortic in origin, whereas in others it is probably dependent on narrowing or occlusion of the orifices of the coronary arteries Excruciating or knife-like pain may be the final symptom before fatal hemorrhage as a result of the rupture of a syphilitic aneurysm

*Signs* —The signs depend upon the location and extent of the lesion and whether we are dealing with aortitis aortic valvular insufficiency or aortic aneurysm In pa

develops and may become permanent. Congestive heart failure occurs in 65 per cent of the cases with auricular fibrillation.

*Roentgen Findings.*—In the early stages of thyrotoxic heart disease, the heart may be normal in size and shape. As the disease progresses, the pulmonary artery salient becomes prominent. In time, there will also be left ventricular and, to a lesser degree, right auricular enlargement. Evidences of congestive failure appear in the later stages of the disease. A hilar dance is noted in many cases.

*Electrocardiographic Findings.*—The electrocardiogram usually reveals sinus tachycardia or some form of arrhythmia, particularly auricular fibrillation, though sometimes paroxysmal tachycardia or flutter. With sinus tachycardia, one may find inversion of the T waves and depression of the ST segments in 1 and 2 and in precordial leads. These changes are usually reversible when the thyroid dysfunction has been corrected.

*Diagnosis and Differential Diagnosis.*—Thyrotoxicosis should always be considered in the diagnosis of any case of cardiac disability. A diagnosis of thyrocardiac disease is based on history of a thyrotoxicosis and evidence of distinct enlargement of the thyroid gland (which is usually nodular). In the more chronic types of toxic adenoma, significant impairment in cardiac function, even congestive failure, may develop without much evidence of disordered thyroid function. Here the possibility of thyrocardiac disease may be suggested by nodular enlargement of the thyroid and unexplained auricular fibrillation. The basal metabolic rate is frequently the determining factor. Protein bound iodine determination and radioactive iodine uptake will establish the diagnosis in the borderline case. The ballistocardiogram and the circulation time (arm to tongue) are additional diagnostic aids.

In the differential diagnosis, one must consider heart failure or hypertension *per se*, polycythemia, coarctation of the aorta, cardiac failure associated with beriberi, and various low grade toxic states, *e.g.*, tuberculosis and neurocirculatory asthenia. Most of these conditions may raise the basal metabolic rate. By careful evaluation and study, however, most of these possibilities may be eliminated.

*Prognosis.*—The prognosis depends on the extent of cardiac damage. Auricular fibrillation and the electrocardiographic findings discussed above often disappear after subtotal thyroidectomy. Striking results are not infrequently obtained by operation even in the presence of congestive heart failure. If the cardiac disability is primarily dependent on other forms of heart disease, the outlook is not so favorable. Even in advanced forms of the latter, however, considerable relief often follows the control of thyrotoxicosis.

*Course.*—The course of thyrocardiac disease is variable and depends on the condition of the thyroid state and the previous condition of the heart. In most cases the cardiac changes revert to normal after the basal metabolic rate returns to normal; however, in some few patients of the older age group and those with long standing hyperthyroidism, some cardiac damage remains. Even after successful operation there is usually evidence of sympathetic overactivity, with a tendency to tachycardia and a mild return of the hyperthyroid state for the rest of the patient's life.

*Treatment.*—First of all, the thyrotoxicosis must be controlled (*see* Chapter 16 for detailed discussion). Then the heart disease must be controlled. In patients with severe cardiac damage and heart failure associated with thyrotoxicosis, propylthiouracil or radioactive iodine will entail less risk than surgery. When the patient is in congestive failure, bed rest, relaxation, sleep, diet low in sodium and high in carbohydrate and protein are the first requisites. The patient should be given digitalis and mercurial diuretics. Larger amounts of digitalis than usual may be necessary because of hyperthyroidism. It is essential that the hyperthyroidism be treated at the same time as the heart disease. After thyroidectomy the auricular fibrillation will usually disappear. If it does not, small doses of quinidine may reestablish a regular sinus rhythm.

MYXEDEMA HEART.—Myxedema heart is rare. Pathologically, the myxedema heart is enlarged with infiltration of the myocardium by a myxomatous material. There may

aneurysms occur in older patients and are due to arteriosclerosis

It is important to differentiate aortic aneurysm from thoracic tumor If the mass is an aneurysm, it is continuous with the vascular pedicle in all roentgen views An aneurysm, furthermore, may pulsate, also the patient's diaphragms move normally and the "sniff test" is negative Angiocardiography will in most cases establish the diagnosis beyond the shadow of a doubt

*Prognosis* — The prognosis depends upon the type of aortitis present In atrophic aortitis, the prognosis is least favorable The over-all picture depends upon the amount of aortic dilatation, its location the absence or presence of coronary ostial involvement, valvular insufficiency, and the type of work performed by the patient There is usually extensive damage and often cardiac failure by the time the disease is recognized The course, therefore is in general progressively downward, and the patient usually dies in from three to five years But some patients may live ten or fifteen years or more

The prognosis is considerably improved if the disease is discovered early and systematic treatment instituted before significant aortic insufficiency develops or there is much encroachment upon the orifices of the coronary arteries Death when it occurs results from either heart failure angina pectoris coronary occlusion intercurrent infection or rupture of an aneurysm

*Treatment* —(*See* Chapter 3)

## THE HEART IN DISEASES OF THE THYROID GLAND

THYROTOXIC HEART DISEASE —The incidence of *thyroid heart disease varies* greatly throughout the world it is however highest where the incidence of toxic adenoma and exophthalmos is high

*Etiology* —The increased demand on the heart from an elevated basal metabolic rate probably contributes to cardiac disability in thyrotoxicosis In patients with hyperthyroidism the cardiac output and blood velocity are increased considerably above normal Some believe, however that it is a *toxic substance released by the thyroid gland* that causes the heart damage

In general, the cardiac disability is likely to be worse in long standing cases of thyrotoxicosis, especially in those *complicated* by arteriosclerosis, hypertension, or rheumatic heart disease Thyrocardiac failure is related to cardiovascular disease in 2 out of 3 cases

*Pathology* —There are no distinct pathologic findings in thyrocardiac disease although the heart is frequently enlarged there is seldom a marked increase in its weight It seems probable that the usual enlargement of the heart is due chiefly to dilatation The *pulmonary artery too is* often dilated in the presence of thyrocardiac disease

*Signs and Symptoms* —The persistence of increased cardiac rate during sleep is one of the earliest and one of the most distinctive signs of thyrocardiac disease This sign is frequently accompanied by palpitation of the heart, tachycardia, and an uncomfortable sensation in the precordium As the thyroid disorder progresses the cardiac rate continues to increase, the patient becomes more and more conscious of his heart and shortness of breath is readily induced by exertion Finally more characteristic manifestations of impaired cardiac function may appear—paroxysmal or continued auricular fibrillation or the onset of congestive heart failure In the older patient angina pectoris frequently occurs

The increased cardiac activity is at once detectable through the exaggerated pulsation of the peripheral vessels, this is most apparent in the neck and in the suprasternal notch The pulsation is full and quick and to a certain extent resembles that of aortic insufficiency The blood pressure shows some increase in the systolic phase whereas *the diastolic phase may be normal or slightly* reduced (thus producing a high pulse pressure) Though the heart is normal in size in the early stages it rapidly becomes enlarged as the hyperthyroid state continues Systolic murmurs are common at the apex especially over the pulmonary area Occasionally the vibration of the chest wall from the accelerated cardiac rate suggests the presystolic thrill of mitral stenosis The circulation time (arm to tongue) is decreased to 8 or 10 seconds As the condition persists, paroxysmal auricular fibrillation

develops and may become permanent Congestive heart failure occurs in 65 per cent of the cases with auricular fibrillation

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MYXEDEMA HEART — Myxedema heart is rare Pathologically, the myxedema heart is enlarged with infiltration of the myocardium by a myxomatous material There may

also be pericardial effusion The cardiac symptoms are almost nil though dyspnea has been noted in a few cases and angina pectoris or congestive failure may occasionally be a complication The pulse rate, however, is slow (40 to 50 beats per minute) and the heart may be enlarged The cardiac output is decreased as is blood velocity, peripheral blood flow, and total blood volume The circulation time is increased to 20 or 25 seconds The teleoroentgenogram shows an enlarged cardiac silhouette, such as is seen in pericardial effusions On fluoroscopy, the cardiac pulsations are seen to be markedly diminished The electrocardiogram shows a low-voltage curve with flattening or inversion of the T wave throughout

*Treatment* —The treatment of myxedema heart consists in correcting the underlying myxedematous condition of the body by the administration of thyroid extract Treatment of this condition must be started very cautiously, since these patients are sensitive to thyroid One may precipitate either angina pectoris or myocardial infarction by the rash use of thyroid No more than 15 to 30 mgm of thyroid a day should be given at first The amount of thyroid given must be regulated not so much by the patient s basal metabolic rate, as by his cardiac response to the drug The treatment of angina pectoris is as previously outlined (*See* page 776) Digitalis must be used when the patient is in heart failure

## CONGENITAL CARDIAC MALFORMATIONS

Congenital heart malformation is a relatively rare cause of cardiac disease It is found in no more than about 3 per cent of all autopsied cases of heart disease In recent years, however surgical procedures to correct a certain number of congenital heart defects have been developed and so the subject has acquired a new interest It has become quite important that an anatomic diagnosis of the type of congenital heart lesion be made in a given case so that one can decide whether any given case is amenable to surgery Such studies have been aided by the use of new diagnostic procedures, *e g*, angiocardiography and catheterization technique

*Classifications* —The older classification of congenital heart malformation, as outlined by Maude Abbott divided this condition into three groups based on the presence or absence of cyanosis Helen Taussig divided congenital cardiac malformation into two groups based on adequate oxygenation for proper growth (*See* Table 45 )

*Etiology* —The etiology of congenital heart malformation is unknown, but several explanations are widely accepted (1) defects in the genes, (2) fetal endocarditis, (3) alcoholism and syphilis in the parents and (4) virus disease in the mother, particularly German measles before the eighth to tenth week of fetal life

*Incidence* —Five per cent of all cases of heart disease in children under two are congenital in origin In patients older than two the incidence is only 0 5 per cent

The most common anomalies in their order of frequency are (1) interauricular septal defect, especially small but patent openings (2) interventricular septal defect

TABLE 45 —CLASSIFICATION OF CONGENITAL HEART DISEASE

*Based on Cyanosis*

*Acyanotic Group* (No connection is present between the greater and lesser circulations)

1 Dextrocardia
2 Persistent right aortic arch
3 Pericardial defects
4 Idiopathic congenital hypertrophy of the heart
5 Coarctation of the aorta
6 Sub-aortic stenosis
7 Double aortic arch
8 Valvular defects such as bicuspid valves pulmonary stenosis etc

*Cyanosis Tardive Group* (Under ordinary circumstances there is a left to right shunt but with increased pressure on the right side the shunt is reversed)

1 Patent ductus arteriosus
2 Interauricular septal defect
3 Interventricular septal defect

*Cyanotic Group* (A right to left shunt is present at all times)

1 Tetralogy of Fallot
2 Eisenmenger complex
3 Tricuspid atresia
4 Common truncus
5 Transposition of the arterial trunks
6 Single ventricle with two auricles

7 Ebstein s anomaly of the tricuspid valve
8 Pulmonary stenosis combined with a septal defect

*Based on adequate oxygenation for proper growth (Taussig)*

*Group I* (Malformations permitting body to receive an oxygen supply sufficient for adequate growth of the individual)
1 Latent ductus arteriosus
2 Interauricular septal defects
3 Interventricular septal defects
4 Eisenmenger complex
5 Aneurysm of the *sinus of Valsalva*
6 Anomalies of the aortic valve and ascending aorta
7 Anomalies of the aortic arch
8 Coarctation of the aorta
9 Dextrocardia with or without situs inversus
10 Ebstein s anomaly of the tricuspid valve
11 Complete A V block and other cardiac arrhythmias

*Group II* (Malformations not permitting the body to receive an adequate oxygen supply for proper growth)
1 Tetralogy of Fallot
2 Tricuspid atresia
3 Common truncus
4 Transposition of the arterial trunks
5 Single ventricle with two auricles

(3) patent ductus arteriosus (4) pulmonary stenosis (5) coarctation of the aorta (6) anomalies of the great veins, (7) complete transposition of the arterial trunks

*Symptoms* — The symptoms of congenital heart disease may be slight in the acyanotic group moderate in the cyanosis tardive group but intense in the cyanotic group In the last two groups the chief symptoms are palpitation precordial pain shortness of breath and signs of arrested development In the more severe forms of congenital heart disease, the symptoms will develop early, death soon follows In the less severe cases the patients may reach adult life with little if any discomfort

*Physical Signs* — In a relatively small group of cases, congenital heart disease may exist without signs the heart is normal in size and no murmurs are heard In most cases however, there are usually one or more of the following signs depending on the type of congenital heart disease dyspnea cyanosis heart enlargement thrills and murmurs It is interesting to note that if we divide the precordial area into two regions by a horizontal line drawn at about the level of the third interspace most of the cardiac signs are found above this line particularly on the left side in the region of the pulmonary artery salient The murmurs are usually loud systolic, and are frequently accompanied by a thrill When heard in the mitral area they are usually the result of transmission The liver may be enlarged as the result of congestive heart failure from right heart strain

*Diagnostic Aids* — In congenital heart disease, roentgen studies, particularly angiocardiography and aortography are essential to diagnosis Cardiac catheterization has probably been the most important diagnostic advance in the study of congenital heart disease From chamber pressure and oxygen studies one can diagnose even the most obscure cases The electrocardiogram is helpful in determining right or left electrical preponderance Circulation times and the determination of oxygen saturation of the arterial blood are also often helpful

*Differential Diagnosis* — The following points favor a congenital origin for heart disease in a child the presence of a heart murmur at birth a loud murmur systolic in time accompanied by a thrill at the pulmonic area cardiac enlargement prominence of pulmonary artery salient and marked right axis deviation in the electrocardiogram (left axis deviation is seen in cyanotic congenital heart disease only with tricuspid atresia or a single ventricle)

Rheumatic heart disease is characterized by a history of repeated respiratory infections a murmur (heard after the age of four years) maximum at the apex and absence of cyanosis, unless accompanied by congestive failure

Usually through angiocardiography, cardiac catheterization the electrocardiogram the case history the location of the murmur and shape of the heart one may arrive at the proper diagnosis

*Individual Lesions* — A *right aortic arch* may occur alone or in association with a *vascular ring* It may give no symptoms whatsoever But if symptoms are present they are usually dysphagia and vomiting These result from encroachment on the esophagus by a portion of the aortic arch or one of the aberrant vessels making up

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5 Transposition of the arterial trunks
6 Single ventricle with two auricles

show an increased pressure and increased oxygen saturation in the right ventricle On exercise the oxygen consumed per liter of ventilation will rise and the oxygen saturation of the peripheral arterial blood will fall A surgical treatment for this defect has been devised but is still in the experimental stage

*Inter-atrial-Septal Defect* —This is a fairly common congenital lesion Patients with this defect often live to old age The defect may be isolated or may occur in conjunction with mitral stenosis (the Lutembacher syndrome) In the latter condition the left auricle is small because it is above the right auricle and blood passes directly from it into the right auricle through the large opening The differential diagnosis between this condition and acquired mitral disease can be made on the basis of the size of the left auricle In uncomplicated interauricular septal defect a systolic murmur is heard in the pulmonic region this is accompanied by an accentuated second pulmonic sound The murmur is not due to the defect in the auricular wall but to the increased work of the right ventricle A systolic thrill may also be felt Twenty per cent of the cases will show a soft blowing diastolic murmur due to a relative dilatation of the pulmonary orifice Arrhythmias and conduction defects are common in this condition One may find auricular fibrillation auricular flutter, or partial A V block all as a result of a marked dilatation of the right auricle Right heart failure occurs often and the patients display a great susceptibility to pulmonary infarction Cyanosis is not present though it may occur eventually upon effort or when infection or heart failure supervenes Marked right ventricular hypertrophy is usually present and the pulmonary artery is large Marked bilateral hilar densities due to increased blood flow are seen on x ray and a hilar dance is characteristic on fluoroscopy The electrocardiogram very commonly shows right-ventricular hypertrophy and right bundle branch block Angiocardiography in this lesion is not ideal because the dye enters the left heart considerably diluted It is best demonstrated by x ray, or by catheterization of the right heart the dye may be put directly into the heart The right and left atria then become dense at about the same time due to flow of dye across the defect Persistent visualization of the right heart when the left auricle contains the dye and marked enlargement of the pulmonary artery are the other angiocardiographic features In catheterization of the heart it is found that the oxygen saturation of the right auricle is above normal The oxygen levels in the right ventricle are higher than normal but below those of the auricle and in the pulmonary artery the oxygen levels are still lower In this case the catheter may be passed into the left auricle where the oxygen saturation is normal but under increased pressure The left ventricle shows the maximum degree of oxygen saturation and pressure On exercise the oxygen consumed per liter of ventilation rises and the saturation of the peripheral blood falls Circulation time will be normal unless heart failure is present Surgery has recently been used to correct the patent interauricular-septal defect Its status is not yet clear

*Patent Ductus Arteriosus* —This is a very important congenital anomaly not because it often occurs but because it can readily be corrected As a result of this anomaly, blood passes from left to right from the aorta to the pulmonary artery through the patent ductus at times the pulmonary flow is twice that of the systemic flow This results in cardiac enlargement with heart failure as the patient grows older Furthermore bacterial endarteritis engrafted upon the patent ductus is not uncommon

*Signs and Symptoms* —No cyanosis or clubbing of the fingers is found The heart may be normal in size or slightly or moderately enlarged The most important sign is the presence of a to-and fro machinery murmur with maximal intensity in the second left intercostal space and a thrill in the same area This thrill may be systolic or both systolic and diastolic Next in order of frequency is a rough systolic murmur in this area This is followed by a high pitched diastolic murmur similar to that heard in aortic insufficiency Occasionally only a systolic murmur may be heard though this has been denied by Taussig The diagnosis should never be

the vascular ring. A diagnosis is made by noting the absence of the aortic knob from its usual position and by means of barium 'swallow,' examining the patient in the right anterior oblique and P-A positions in order to see whether there is encroachment upon the esophagus by aberrant vessels or an abnormal aortic arch. It is important to diagnose this condition since the abnormal vascular ring is amenable to surgery and all symptoms can be relieved by proper surgical intervention.

*Coarctation of the Aorta.*—This fairly common abnormality may be divided into two types—the infantile (rare) and adult types. In the infantile type there is a narrowing of the whole isthmus between the left subclavian artery and the ductus arteriosus. At times the proximal arch itself may also be involved. These patients do not have a very long life because, in addition to this anomaly, other congenital defects are usually present. The second or adult type of coarctation of the aorta consists of a localized constriction of the aorta at or just below the insertion of the ductus arteriosus (rarely above that point). Though called the adult type, it is always a prenatal condition, but it is the usual type that is found after the first year of life. The narrowing may be slight, moderate or almost complete.

*Symptoms and Signs.*—The adult type of coarctation of the aorta seldom causes symptoms or signs until the patient is above 20 years of age. The signs and symptoms result from hypertension in the upper part of the body and hypotension in the lower part. In addition, murmurs are present over the various parts of the chest; these are due to the compensatory dilatation of the collateral blood vessels. The murmurs are usually heard over the internal mammary and intercostal arteries and over the scapular vessels. Femoral pulsations are decreased or absent, and the blood pressure of the lower extremities may be very low. There is also a delay in the propagation of the femoral pulse as compared to the brachial pulse.

The *roentgen findings* in coarctation of the aorta are characteristic: absence of the aortic knob, erosion of the undersurface of the ribs, and narrowing of the descending aorta at the point of coarctation in the left oblique position. *Angiocardiography* and *aortography* serve to confirm the diagnosis and determine the site and type of coarctation.

The complications of coarctation of the aorta are those of hypertension: dissecting aneurysm with rupture of the first portion of the aorta, subarachnoid hemorrhage or cerebral apoplexy, congestive heart failure, subacute bacterial endocarditis (when a bicuspid aortic valve complicates the coarctation).

Except for the infantile type, the prognosis is fairly good. Many of these patients have a normal life span, some, however, die of the complications mentioned above.

This condition may now be cured by surgery—excision of the coarctation with an end-to-end anastomosis of the aorta. In some cases, however, because of the size of the coarctation, grafts have been used to correct the defect. In other cases other blood vessels have been used to bridge the gap because of the large area of coarctation. In good hands the mortality rate is low and the results are satisfactory.

*Interventricular Septal Defect.*—This is a common congenital anomaly. It often occurs alone but other defects may be found. The patient has usually a normal life span. If the defect is not too large, there is little cardiac embarrassment. But in most cases it usually results in increased cardiac work because of the left to right shunt. Physiologically, there is cardiac enlargement with right and left ventricular hypertrophy. This eventually leads to combined right and left heart strain, resultant symptoms and changes in heart size. On examination, the heart appears to be enlarged and globular. It tends to get larger as the patient gets older. In the third intercostal space, just to the left of the sternum, there is usually present a systolic thrill accompanied by a rough systolic murmur transmitted to the apex and base. No cyanosis is present unless heart failure or pulmonary infection supervenes. Circulation time is normal. *Angiocardiographic* findings usually show renewed visualization of the right ventricular chamber after it is emptied and the left ventricle has filled. *Catheterization* will

suggests left ventricular hypertrophy but it is made up entirely of the hypertrophied right ventricle In the right anterior oblique position there is no fullness of the pulmonary conus In the left anterior oblique position the pulmonary window is very clear and the bifurcation of the trachea is easily seen The left ventricle is not enlarged but may in the left anterior oblique position overlap the spine probably because the enlarged right ventricle pushes back the left chamber

*Electrocardiography* —The electrocardiogram invariably shows right axis deviation Right ventricular hypertrophy verging on right bundle branch block is present and is best seen in the precordial leads

*Exercise Test* —By exercising the patient one may reduce the pulmonary circulation even more than it usually is in such a case There is a fall in the oxygen consumed per liter of ventilation as well as in the oxygen content of the peripheral blood This helps differentiate the tetralogy of Fallot from the Eisenmenger complex in which the pulmonary blood flow is unaffected or increased after exercise

Right heart *catheterization* though sometimes useful is usually unnecessary It will demonstrate the septal defect increased right ventricular pressure and a very low pulmonary artery pressure

*Treatment* —There are three operations now performed to increase the deficient pulmonary blood flow All three are designed to increase the blood flow through the lungs and so overcome the cyanosis the attendant polycythemia and other complications The Blalock Taussig operation consists in attaching the subclavian artery to the pulmonary artery The Potts operation induces increased pulmonary circulation by side to side anastomosis of the aorta and the pulmonary artery The Brock operation attacks the seat of the trouble at the pulmonary valve itself by overcoming the stenosis there by direct cutting of the valve Surgery is the treatment of choice

*Eisenmenger Complex* —This condition is similar to the tetralogy of Fallot only the pulmonary valve is not stenosed and the pulmonary artery is normal or actually dilated Patients with this condition become cyanotic not at birth but later in life, and the cyanosis is much less marked than in the tetralogy of Fallot Furthermore, the clubbing of the fingers is less marked The cyanosis usually becomes conspicuous when the patient is adolescent The cardiac findings are these normal or accentuated second pulmonic sound a systolic murmur is often heard over the pulmonic area absence of heart concavity (on x ray) prominent pulmonary artery normal hilar shadows and occasionally some hilar dance ' The electrocardiogram shows right-axis deviation The pulmonary blood flow by *catheterization* is normal and does not decrease after exercise The oxygen saturation of the arterial blood is decreased after exercise One must differentiate between the Eisenmenger complex and pulmonary stenosis with interauricular-septal defect The difference is that, in pulmonary stenosis with interauricular-septal defect the lung fields are clear with decreased hilar pulsation

Patients with Eisenmenger complex usually live to the third or fourth decade and die of an intercurrent illness

## CATHETERIZATION IN CONGENITAL HEART DISEASE *

In the presence of an auricular septal defect, blood flows from the left to the right auricle The venous catheter is helpful in demonstrating arterial blood in the right auricle or in passing through the septal defect

In uncomplicated ventricular septal defect arterial blood flows from the left to the right ventricle Venous catheterization may serve to demonstrate an increased oxygenation of blood in the right ventricle as compared with that in the right auricle Pressures in the right ventricle and in the pulmonary artery may be in excess of normal

In the tetralogy of Fallot (pulmonary stenosis interventricular septal defect overriding or dextroposition of the aorta and right ventricular hypertrophy) some venous blood is shunted through the septal defect

* After C D Marple Postgraduate Med March 1951

made clinically unless one hears the machinery murmur or at least the double murmur

*Roentgen* study reveals a normal sized or slightly or moderately enlarged heart, a slight prominence of the pulmonary artery and moderately prominent hilar shadows A hilar dance may be observed *Angiocardiography* shows filling of the pulmonary artery after the right ventricle has emptied and as the left ventricle is filled and dye is going out into the aorta At times one can actually visualize the ductus However a much more common finding is a traction aneurysm of the first portion of the descending aorta at the site of insertion of the ductus

The electrocardiogram will often be normal However occasionally left axis or right axis deviation is seen

*Catheterization* reveals an increased oxygen saturation in the pulmonary artery at the level of the patent ductus and an increase in pressure in the right ventricle and pulmonary artery The oxygen consumed per liter of ventilation rises on exercise and the oxygen saturation of the peripheral blood is unchanged Circulation time is normal

*Treatment* —The treatment for this condition is surgical The ductus may be ligated tied off and wrapped in cellophane or cut and transfixed Surgery has been performed with amazingly good results even in the presence of subacute bacterial endarteritis It is worthy of note that a systolic *murmur may persist even after adequate* and proper surgery

*Cyanotic Congenital Heart Disease* —The most common cyanotic lesions are (1) the tetralogy of Fallot (2) Eisenmenger s complex (3) tricuspid atresia (4) common truncus (5) transposition of the arterial trunks and (6) Taussig heart These may be divided into three groups the first is characterized by a diminished pulmonary blood flow as in the tetralogy of Fallot tricuspid atresia and pulmonary stenosis the second is characterized by difficulty in getting oxygenated blood to the periphery through the systemic circulation as in transposition of the arterial trunks aortic atresia and anomalies in venous return the third is characterized by difficulty in aerating the blood in the lung This last group is probably epitomized in part by the Eisenmenger complex, though this has not yet been proved

There are four principal adaptations to congenital cyanotic heart disease (1) polycythemia, with increased production of red cells under the stimulus of anoxia of the bone marrow (2) hyperventilation for added oxygenation (3) minimal oxygen hemoglobin dissociation at the lower levels of oxygen saturation (4) decreased basal metabolic rate *with decreased demand for* oxygen by the tissues

*Tetralogy of Fallot* —This condition embraces (1) pulmonary stenosis or atresia (2) right ventricular hypertrophy (3) interventricular septal defect and (4) overriding of the aorta In 25 or 30 per cent of the cases there is a right aortic arch This is an accompanying anomaly and is not the same as overriding of the aorta Victims of this condition do not usually live beyond puberty though some may reach adult life (oldest victim died at 64) Death usually results from cerebral thrombosis or anoxemia

*Symptoms* —Cyanosis usually marked appears at birth or shortly thereafter and is severe Clubbing of the fingers and toes and polycythemia are present Squatting as a reaction to fatigue and lack of oxygen is characteristic as is markedly reduced exercise tolerance

*Signs* —The heart is normal in size or slightly *enlarged* A *rather harsh systolic* murmur, with a systolic thrill is present in the third to fourth left intercostal space along the left border of the sternum The murmur is frequently transmitted to the back of the chest and the vessels of the neck In a few cases there is no murmur The pulmonary second sound is faint or absent leading often to a pure second sound at the base

*X Ray and Fluoroscopy* —The characteristic finding is unusually clear lung fields with only fine vascular markings Some cases manifest the so called wooden shoe heart The left border of the heart is usually straight or concave The apex is upturned and the silhouette somewhat

the effusion in the pericardial sac is chiefly serous or fibrinous The latter type may develop into chronic pericarditis in which there are adhesions between the pericardium and the heart and between the pericardium and other structures

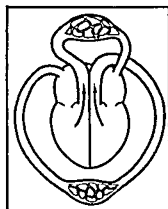
*Etiology* —The etiology of pericarditis is extremely varied There are, however many important causes rheumatic fever pneumonia tuberculosis chronic nephritis and coronary occlusion Rheumatic fever is the most common etiologic factor The pericarditis may develop at any stage of the disease but occurs most frequently during acute exacerbations The incidence as determined by necropsy findings is very high in those who succumb from rheumatic heart disease during the first and second decades of life This would indicate that the pericardium is very commonly involved in the more acute and rapidly progressing forms of rheumatic heart disease A pericarditis not infrequently occurs during the course of acute infections particularly pneumonia It occasionally complicates scarlet fever and may result from invasion of the blood stream in puerperal infection osteomyelitis, furunculosis gonorrhea and other types of sepsis Although the pericarditis which is associated with pneumonia may be of hematogenous origin it is usually produced by direct extension of the infection from a pneumonic lower lobe particularly the left or from an empyema In tuberculosis also the pericardium is invaded by direct extension from the pleura lung or mediastinal lymph nodes Any infection of the neighboring structures including the ribs sternum vertebræ or even of the abdominal viscera may extend to the pericardium The pericarditis of chronic nephritis is usually a terminal event such as is seen occasionally in the terminal stages of various other chronic diseases In rare instances the pericardium is involved by malignant tumors generally metastatic but at times by direct extension from adjacent structures The pericardial changes incident to coronary occlusion are very important because the associated pericardial rub is the most distinctive sign of cardiac infarction (but unimportant from the standpoint of pericarditis) A nonspecific or cryptogenic pericarditis may be due either to a virus infection or to an allergic response to a bacterial antigen in the upper respiratory tract

The varied nature of the etiologic factors permits pericarditis to occur at almost any age Cases have been reported in newborn infants The incidence is perhaps highest during childhood and early adult life because of rheumatic fever The disease is more prevalent in the male sex

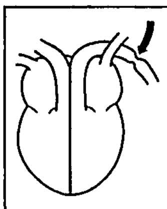
*Pathology* —The effusion varies in amount and rate of formation It may be serofibrinous hemorrhagic or purulent depending on the type of the primary disease A hemorrhagic effusion is generally associated with tuberculosis or malignancy and a purulent exudate with pneumonia or a blood stream infection caused by some pyogenic organism A clear straw-colored fluid is associated with the so-called nonspecific type of pericarditis The amount of fluid ranges from a few hundred cubic centimeters to 2 liters or more The largest effusions are seen in tuberculosis and not in rheumatic fever more particularly in the former There is a varying amount of fibrinous exudate which forms ridges or presents an irregular shaggy appearance The pericardial layers are congested and perhaps show hemorrhagic areas In the cases with a purulent exudate there is often a granular appearance and sometimes distinct erosions The parietal layer is frequently thickened and may be of a leathery consistency In the more chronic forms the exudate may be separated into pockets by the formation of adhesions between the visceral and parietal layers of the pericardium The outer layers of the myocardium are usually involved to a certain extent

In the pericarditis which is associated with rheumatic fever there is invariably a general invasion of the myocardium which may be extensive

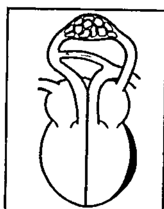
With the accumulation of fluid in the pericardial sac several things will occur—first increased venous pressure then failure of proper diastolic filling of the heart This may result in decreased cardiac output with salt retention and this eventually in heart failure Furthermore the pericardium may become enlarged and encroach upon the lung and interfere with its function



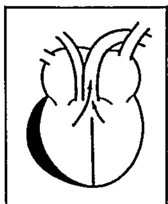
Normal



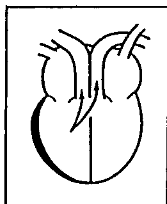
Coarctation of the aorta



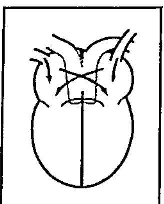
Patent ductus arteriosus



Tetralogy of Fallott



Eisenmenger complex



Interauricular septal defect

Fig 139 —Diagrammatic representation of the blood flow through the heart great vessels and lungs in the normal heart and in the common congenital defects (Courtesy of C D Marple and Postgraduate Medicine )

into the aorta The venous catheter may pass through the stenotic pulmonary valve into the pulmonary artery or may pass through the septal defect into the over riding aorta Pressure in the right ventricle is elevated that in the pulmonary artery is usually low Oxygenation of the peripheral blood is deficient due to admixing

In the Eisenmenger complex similar to the tetralogy except for absence of pulmonary stenosis pressure in the pulmonary artery is elevated rather than reduced and entry into this artery is ordinarily not obstructed

In patent ductus arteriosus the flow of blood is from the aorta to the pulmonary artery Venous catheterization demonstrates arterial blood in the pulmonary artery (oxygen content in pulmonary artery greater than that in right ventricle) Pressures in the right auricle the right ventricle and the pulmonary artery are elevated

In simple pulmonary stenosis, pressures in the right heart are increased but that in the pulmonary artery is decreased Entrance into the pulmonary artery is obstructed Systemic and pulmonary blood flows are reduced equally

## PERICARDIAL DISEASE

*Acute Pericarditis* —Pericardial effusion is of two types (1) noninflammatory or (2) inflammatory The type depends on whether

the effusion in the pericardial sac is chiefly serous or fibrinous The latter type may develop into chronic pericarditis in which there are adhesions between the pericardium and the heart and between the pericardium and other structures

*Etiology* — The etiology of pericarditis is extremely varied There are however many important causes rheumatic fever pneumonia tuberculosis chronic nephritis and coronary occlusion Rheumatic fever is the most common etiologic factor The pericarditis may develop at any stage of the disease but occurs most frequently during acute exacerbations The incidence as determined by necropsy findings is very high in those who succumb from rheumatic heart disease during the first and second decades of life This would indicate that the pericardium is very commonly involved in the more acute and rapidly progressing forms of rheumatic heart disease A pericarditis not infrequently occurs during the course of acute infections particularly pneumonia It occasionally complicates scarlet fever and may result from invasion of the blood stream in puerperal infection osteomyelitis furunculosis gonorrhea, and other types of sepsis Although the pericarditis which is associated with pneumonia may be of hematogenous origin it is usually produced by direct extension of the infection from a pneumonic lower lobe, particularly the left or from an empyema In tuberculosis also the pericardium is invaded by direct extension from the pleura lung or mediastinal lymph nodes Any infection of the neighboring structures including the ribs sternum vertebrae or even of the abdominal viscera may extend to the pericardium The pericarditis of chronic nephritis is usually a terminal event such as is seen occasionally in the terminal stages of various other chronic diseases In rare instances the pericardium is involved by malignant tumors generally metastatic but at times by direct extension from adjacent structures The pericardial changes incident to coronary occlusion are very important because the associated pericardial rub is the most distinctive sign of cardiac infarction (but unimportant from the standpoint of pericarditis) A nonspecific or cryptogenic pericarditis may be due either to a virus infection or to an allergic response to a bacterial antigen in the upper respiratory tract

The varied nature of the etiologic factors permits pericarditis to occur at almost any age Cases have been reported in newborn infants The incidence is perhaps highest during childhood and early adult life because of rheumatic fever The disease is more prevalent in the male sex

*Pathology* —The effusion varies in amount and rate of formation It may be serofibrinous hemorrhagic or purulent depending on the type of the primary disease A hemorrhagic effusion is generally associated with tuberculosis or malignancy, and a purulent exudate with pneumonia or a blood stream infection caused by some pyogenic organism A clear straw-colored fluid is associated with the so-called nonspecific type of pericarditis The amount of fluid ranges from a few hundred cubic centimeters to 2 liters or more The largest effusions are seen in tuberculosis and not in rheumatic fever, more particularly in the former There is a varying amount of fibrinous exudate which forms ridges or presents an irregular shaggy appearance The pericardial layers are congested and perhaps show hemorrhagic areas In the cases with a purulent exudate there is often a granular appearance and sometimes distinct erosions The parietal layer is frequently thickened and may be of a leathery consistency In the more chronic forms the exudate may be separated into pockets by the formation of adhesions between the visceral and parietal layers of the pericardium The outer layers of the myocardium are usually involved to a certain extent

In the pericarditis which is associated with rheumatic fever there is invariably a general invasion of the myocardium which may be extensive

With the accumulation of fluid in the pericardial sac several things will occur—first increased venous pressure then failure of proper diastolic filling of the heart This may result in decreased cardiac output with salt retention and this eventually in heart failure Furthermore the pericardium may become enlarged and encroach upon the lung and interfere with its function

If the fluid in the pericardial sac becomes infected, the contiguous organs may become involved. Then adhesions may form between the heart and the pericardium. These adhesions may produce either the so-called superior mediastinal syndrome (in which the superior vena cava, the pulmonary artery, and the aorta may become involved in adhesions with resultant interference with the proper functions of these blood vessels) or the inferior mediastinal syndrome (in which the inferior vena cava is entrapped in adhesions with resultant liver enlargement and eventually, perhaps, a syndrome that looks very much like cirrhosis of the liver with ascites). Finally there may *be adhesions between the parts of the heart* itself, adhesions involving ventricle and auricle and so interfering with heart function. Adhesions may also occur between pericardium and any of the surrounding structures.

*Symptoms.*—The symptoms vary with the nature of the primary infection, the character of the onset of the pericardial involvement, and the extent and rate of accumulation of the effusion. In rheumatic fever the arthritis may be the outstanding clinical manifestation in the beginning, and *the pericarditis, particularly when painless,* not suspected until the onset of dyspnea. The pericarditis may, on the other hand, be *the first significant sign of a bout of rheumatic fever* and, because of the pain, be recognized early. In other instances the effusion into the pericardium is of short duration and never of sufficient extent to embarrass the heart or produce evident pressure signs in the lungs. Under these circumstances the condition may readily escape detection unless attention is focused on the heart through the discovery of a *friction rub. The pericarditis of pneumonia* and other pyogenic infections is likely to be overshadowed by the primary disease. In tuberculosis the onset may be very insidious and the patient may not consult his physician until he suffers from symptoms of cardiac embarrassment.

Pain and shortness of breath are the chief symptoms. The pain may precede the shortness of breath or they may be *associated.* In some cases there is no pain and the dyspnea is the outstanding complaint. The pain of pericarditis may be sharp or of a pressure type and may be located in either the precordial or the substernal *regions.* It may be referred to the arms or to the epigastrium (through the phrenic nerves) (sometimes the entire abdomen), especially in children. This pain may become worse on deep breathing movements or lying down. It may be alleviated by sitting up or leaning forward. Dyspnea may be a very prominent feature, especially when the distended pericardial sac compresses lungs, bronchi and trachea. In the more advanced stages the dyspnea is associated with extensive engorgement of the liver and edema *of the extremities or dependent parts of the* body. The patient at this stage is obliged to sit up and is more comfortable when leaning forward. There is not infrequently an irritating cough, occasionally dysphagia from pressure on the esophagus and in rare instances aphonia through compression or irritation of the recurrent laryngeal nerve. The patient is restless and often unable to sleep except with the help of drugs. In the later stages delirium and even coma may occur. The fever varies with the primary disease. It is generally high in pneumonia *and sepsis and occasionally a prominent* feature in rheumatic fever and nonspecific pericarditis.

*Signs.—At the beginning the most characteristic* finding in pericarditis is the friction rub. This is usually of a to-and-fro character and in most cases is best heard in the second to fourth intercostal spaces to the left of the sternum. The friction rub may last from a few hours to a few days and may then disappear. It usually disappears when fluid accumulates or adhesions form, but it may sometimes be elicited by turning *the patient slowly from side to side to separate* the parietal from the epicardial surface. It may also be noted at the same time that the heart sounds are distant and muffled. This may be helpful especially if the patient is a thin chested one. There will be an increase in the area of deep cardiac dullness. There will often be an extension of the area of dullness at the base of the heart in the first and second interspaces to the right and left of the sternum. This area of dullness fur-

thermore will shift with change from the recumbent to the upright position The shape of the area of cardiac dullness while the patient is sitting is pear like it becomes more globular when the patient lies down The apex beat may be neither visible nor palpable under these circumstances Furthermore a pulsus paradoxus may appear In this situation there will be a decrease in volume of the pulse with inspiration and an increase in the pulse volume during expiration Furthermore there will be depression of the liver this being due to two factors—accumulation of blood in the liver (due to the constriction of the hepatic veins) and pericardial effusion (the weight of which may depress the liver) Increased venous pressure will also be noted In addition there will be compression of the lung by the pericardial effusion Ewart s sign may be found on the left side under these circumstances (dullness and bronchial breathing) But, in the presence of a large effusion this sign may be obtained bilaterally Cyanosis may also be present The circulation time in pericarditis will vary with the heart size In the presence of a small heart with increased venous pressure, the circulation time is little if at all altered The slight increase in circulation time may be due to interference with the entrance of the test substance into the right auricle by the increased venous pressure If the heart is enlarged however there will be an increase in the circulation time

Pericardial tap may be performed to get fluid for culture and cell study to treat cardiac tamponade, to inject air for diagnostic purposes or to inject antibiotics locally The aspirated fluid will be bloody in tuberculous pericarditis and serofibrinous in rheumatic heart disease It will be clear and straw colored in the nonspecific type of pericarditis and purulent in septic pericarditis

*Roentgen Signs* —In pericarditis with effusion there is symmetrical enlargement of the cardiac silhouette At times this enlargement is difficult to differentiate from dilatation of the heart as the result of hypertensive or syphilitic heart disease or from auricular fibrillation with enlargement of the right auricle and symmetrical enlargement of the cardiac silhouette or tricuspid stenosis or regurgitation with enlargement of the right auricle Myxedema heart may also be a difficult differential-diagnostic roentgen finding The earliest sign is a bulging in the dependent portion of the pericardial sac This is best seen on fluoroscopic examination in the lateral view Later as the fluid accumulates the cardiac shadow fills out in the first and second interspaces and the normal curve particularly along the left border of the heart is eliminated At this time a definite alteration in the shape of the cardiac shadow is apparent with the change from the recumbent to the upright position Fluoroscopically diminution in amplitude of the cardiac pulsation can be observed or complete absence of these pulsations when the effusion is extensive This is a very important sign of pericardial effusion and helps differentiate it from heart enlargement

Recently, angiocardiography has added another diagnostic tool to the roentgen study of pericarditis With it one may determine heart size inside the pericardial effusion and at times determine the thickness of the pericardium and (though seldom) the sites of vascular obstruction secondary to pericarditis

*Electrocardiographic Signs* —In the acute stage of pericarditis the electrocardiogram shows ST segment elevation in all leads, with preservation of the normal QRS complex At times the ST segment may be elevated only in Leads I and II and at times in Leads II and III and not in the precordial leads Again the elevation may be present in any 3 of the 4 leads taken Significant Q waves however have never been noted In time the ST-segments will return to the base line and this will be followed by T wave inversion in all leads These T wave inversions will return to normal as soon as the pericarditis has been healed In tuberculous pericarditis the stage of ST elevation is rarely noted and it is the inverted T wave which is the characteristic one in this condition Auricular fibrillation is also common with tuberculous pericarditis due to tuberculous involvement of the auricular muscle Occasionally there may be other electrocardiographic changes but they are not

characteristic or pathognomonic of pericarditis

*Differential diagnosis* among the various types of pericarditis with effusion is not often difficult It is based upon case history, symptoms, physical signs x ray study, the electrocardiogram, and pericardial tap The following differential-diagnostic features may be helpful

| *Tuberculosis* | *Rheumatic Heart Disease* |
|---|---|
| 1 Effusion large and bloody | 1 Effusion small and serofibrinous |
| 2 Patient comfortable | 2 Patient sick because of heart involvement and pancarditis |
| 3 Temperature 101 to 102 F | 3 Temperature variable |
| 4 No murmurs | 4 Murmurs present |
| 5 Blood picture normal or shows leukopenia with neutrophilia or leukocytosis | 5 Blood picture shows leukocytosis |
| 6 Large heart silhouette without heart failure lung fields uncongested but may show lesions of tuberculosis | 6 Large heart silhouette congestion of the lungs due to heart failure |
| 7 Heart size normal after pericardial tap pericardium thickened when demonstrated by air injection | 7 Heart size large after pericardial tap pericardium thin when demonstrated by air injection |
| 8 Tubercle bacilli may be isolated from aspirated fluid | 8 No organism can be isolated |
| 9 History of tuberculosis | 9 History of rheumatic fever |

The nonspecific or cryptogenic type of pericarditis usually has a characteristic acute onset, with evidences of an upper respiratory tract infection and a rapid course At times, a pericardial tap may be necessary to confirm the diagnosis The neoplastic diseases including Hodgkin's disease and leukemia may produce pericarditis due to metastatic lesions and this diagnosis is made by finding lesions elsewhere Presence of uremia with pericarditis will usually help confirm this diagnosis Pericarditis in myocardial infarction may be diagnosed by the presence of the typical electrocardiographic changes of myocardial infarction superadded to those of pericarditis In differentiating the pericarditis of myocardial infarction from other types of pericarditis, it is important to note that, in the former the friction rub the rise in temperature, and the rise in sedimentation rate occur from 24 to 48 hours after the onset of pain whereas in the latter these appear as soon as the pain is noted Rupture of an aortic aneurysm into the pericardium can be diagnosed by the finding of blood in the pericardial sac In rare cases only is pericarditis due to trauma or syphilis In about 10 per cent of the cases, no known cause can be demonstrated even at autopsy

*Prognosis* —The prognosis varies with the nature of the primary condition and the character of the effusion In many instances, in rheumatic fever the fluid is slight in amount and disappears in a few days Even with extensive effusion it is seldom necessary to aspirate the pericardial sac for the effusion is ordinarily of a serous character, rapidly absorbed The amount of myocardial and endocardial damage produced by the rheumatic involvement is more important, generally speaking than the pericarditis In tuberculous pericarditis the onset is more insidious and the course often prolonged Repeated aspirations of the fluid may be necessary Furthermore, because of the chronicity there is greater tendency to the subsequent formation of extensive adhesions In septic pericarditis the prognosis depends on isolating the organism and instituting proper antibiotic therapy The prognosis in nonspecific or cryptogenic pericarditis is excellent since most reported cases have made complete recovery In uremia the presence of a pericarditis has a bad prognostic significance since it is often a terminal event as it may be in other conditions

*Treatment* —Treatment is directed primarily toward the underlying condition and conservation of the cardiac function The patient is confined to bed and relaxation and sleep are promoted The diet should

be simple and meet the body's requirement The application of an icebag to the precordium frequently gives relief from opression and pain and reduces the cardiac rate It may possibly retard the progress of the effusion Morphine is frequently required in severe cases for relief of pain Pericardial tap when indicated as outlined above is done in the following manner It is first imperative that the patient be properly prepared He should be given morphine sulphate ½ hour before the tap If he is restless or uncooperative it is better not to do the tap for a sudden jerk on the patient's part may mean instant death Pericardial fluid should be removed with a syringe * As much as 1800 cc of fluid may be withdrawn in an hour and a half It is possible then to inject air into the pericardial sac to obtain an idea of the heart size and the thickness of the parietal pericardium The injection of air may also actually help prevent formation of adhesions between the layers of the pericardium One may also tap through the xyphoid process by directing the needle upward and inward However by this method one may injure the posterior descending branch of the right coronary artery One may also approach the effusion posteriorly below the angle of the left scapula This is feasible if the effusion is large and not purulent One may also tap to the right of the cardiac silhouette if the effusion is large The danger is that one may penetrate and tear the right auricle which is relatively thin

One may also use the general supportive measures that have been outlined In rheumatic pericarditis tapping is rarely required except for diagnostic purposes The effusion rarely exceeds 500 cc It almost never causes tamponade and is usually absorbed as the patient improves Salicylates may promote the absorption of the effusion as it does in the joints but this is still a highly debatable point The question of the use of ACTH and cortisone is not settled at this time however on the basis of the reports to date it would seem that pericarditis may respond rather rapidly to both of these substances

Until recently 85 out of 100 victims of tuberculous pericarditis died and only 15 recovered In general the less they were tapped the better they did unless tamponade was developing This was true whether the tuberculous pericarditis was primary or secondary However, the use of streptomycin and paraaminosalicylic acid promises a higher cure rate

The treatment for purulent pericarditis in the past was surgical drainage This cured however only about 15 per cent of the patients At present, antibiotics have reduced the mortality rate Antibiotics are given both systemically (parenterally) and locally in the treatment of purulent pericarditis The choice of antibiotic depends on the organism found and its resistance to the various antibiotics available There is no specific treatment for the azotemic pericarditis at the present time except the treatment of the underlying azotemia Recently nonspecific pericarditis has been treated with aureomycin and chloromycetin

*Chronic (Adhesive) Pericarditis —Etiology* —The formation of adhesions between the heart and the pericardium or the pericardium and the surrounding structures may result from tuberculosis which is the most frequent cause of this condition rheumatic fever healed septic pericarditis and in some cases nonspecific infections After myocardial infarction one may find localized adhesions between the pericardium and the heart at the site of the infarct This may sometimes be helpful in preventing cardiac rupture

*Pathologic Physiology* —There is a marked variation in the extent of the adhesions The simplest form is represented by one or more localized adhesions between the parietal and the visceral layers of the pericardium This may in no way interfere with the cardiac function and is therefore of no clinical significance In other instances the adhesions between the heart and the pericardium are more extensive and may entirely obliterate the pericardial cavity (concretio cordis) In such cases the pericardium is usually thickened and contracted and possibly presents areas of calcification The adhesions are dense and not infrequently attached to the chest wall the diaphragm and the mediastinal structures Adhesions around the great vessels cause

* The site of choice for entry is 1 to 2 cm to the left and below the left outer edge of the cardiac silhouette as determined by percussion or preferably by roentgen study

severe disturbances. The superior mediastinal syndrome occurs when there is constriction around the superior vena cava. Cyanosis, increased venous pressure, and edema of the face result. If the pulmonary artery is involved, right heart strain with *cor pulmonale* supervenes. The inferior mediastinal syndrome occurs when adhesions surround the inferior vena cava and cause hepatomegaly, ascites, and edema of the legs. In rare instances, the entire heart may be encircled by constricting bands. This prevents diastolic filling and results in *decreased minute volume* and reduced exercise tolerance. In such a case the adhesions are thick and constrictive. The more extensive the adhesions the greater the handicap placed on the heart. This handicap may lead ultimately to marked cardiac enlargement and failure. The heart is not infrequently hypertrophied and dilated to an extreme degree. In tuberculous pericarditis the heart is small and the adhesions are thick. Most of the cardiac silhouette is made up of the adhesions or thickened pericardium. This is in contrast to the rheumatic pericarditis in which the adhesions are thin and the heart is large.

*Symptoms.*—The symptoms of chronic pericarditis vary with the type and extent of the adhesions. If the adhesions are small, there are no symptoms. The presence of the adhesions may be suspected because of a history of pericarditis or cardiac infarction but their presence is not really established until necropsy. The symptoms of more widespread adhesions are in general those of gradual impairment in cardiac function and finally of congestive failure. Recurrent ascites is the most prominent feature in some cases although there are generally extensive structural changes in the heart. The ascites is out of proportion to the degree of impairment of cardiac function. It is to be explained by portal obstruction secondary to stenosis of the hepatic veins or inferior vena cava by the pericardial adhesions.

*Signs.*—If the adhesions are thin there may be no signs indicative of pericarditis. However, in the presence of extensive pericardial adhesions there will develop disturbances in cardiac *function* with resultant signs of congestive failure such as dyspnea, cyanosis and perhaps edema. In some cases *Broadbent's* sign may be found. This consists of a systolic retraction of the chest wall laterally in the seventh to ninth intercostal spaces. Other areas of retraction may exist around the apex and in the second to fourth left intercostal spaces anteriorly. Retraction of the chest about the apex may occur in any condition where there is heart enlargement. Therefore lateral wall retractions are more significant than anterior ones but they should always be interpreted in the light of the case history and other findings. Diastolic shock is a common symptom of adhesive pericarditis. This occurs because, during systole, the adhesions are made taut and with diastolic relaxation the heart rebounds against the chest wall. It is interesting to note that both chest wall retraction and diastolic shock are more likely to be found in rheumatic adhesive pericarditis than in the tuberculous variety. In the latter, we usually find a silent heart and the above mentioned signs are not seen. Lack of mobility of the heart due to the presence of extensive adhesions may be demonstrated by physical examination. Visible collapse of the veins during diastole with distention during systole may also be noted in many cases. Unilateral or bilateral venous obstruction giving rise to edema, cyanosis, and prominent venous channels in the upper or lower half of the body or in one of the limbs may also be present. This is more common in tuberculous pericarditis. Obstruction of the hepatic veins with perihepatitis may also be found (Pick's disease). This may result in pseudo cirrhosis with normal liver function or with enlarged liver and ascites. This condition may be complicated by a polyserositis and perihepatitis called Concato's disease. The latter may be independent of Pick's disease in some instances. In patients with rheumatic heart disease there will be endocardial lesions with varying murmurs depending upon the valves involved. However, mitral and tricuspid insufficiency may occur in the later stages of concretio cordis with the usual murmurs accompanying the lesions. Paradoxical pulse may also be found under these conditions. Finally, the additional signs

which may be found are those of congestive failure

*Roentgen Signs.*—X-ray and fluoroscopic study will show decreased or absent cardiac pulsations and a ragged outline of the periphery of the cardiac silhouette due to adhesions. These adhesions may be accentuated by forced breathing. Furthermore, the excursions of the diaphragm may be curtailed or the diaphragm may forcibly be pulled upward with each contraction of the heart. The presence of calcification in the pericardium is of course pathognomonic of adhesive pericarditis. By x-ray one may also demonstrate the absence of mobility of the heart previously described under physical signs.

Roentgenkymography will be helpful in establishing the exact amount of cardiac pulsation and may be useful in determining how marked the decrease in cardiac pulsation actually is. The recent addition of angiocardiography is also helpful in making the diagnosis since it is possible by use of contrast media in the heart chambers to demonstrate the thickening of the pericardium.

*Electrocardiographic Findings.*—By the use of the electrocardiogram one may also help determine the fact that the heart is fixed in the mediastinum. The electrocardiogram if taken with the patient lying first on his back, then on the right side and finally on his left side will demonstrate no significant alteration in the ventricular complexes in the presence of a pericarditis with adhesions. In the normal person there will be an alteration in the electrical axis when he is shifted from side to side and from the recumbent to the erect posture. This type of fixation of the heart is most often seen in tuberculous mediastino pericarditis. Other findings in the electrocardiogram are not characteristic but may be suggestive of pericarditis with adhesions (inverted T waves in all leads, for example, and a low amplitude of the QRS complexes in both limb and precordial leads).

*Differential Diagnosis.*—Adherent pericarditis should be suspected in every relatively young individual with marked cardiac enlargement and particularly in those with an associated ascites. The history of a previous pericarditis and of tuberculosis or other forms of pulmonary infection is important. The diagnosis in certain instances is fairly readily established on the basis of a distinct fixation of the heart and the demonstration of adhesions by the roentgen ray. Signs are often indefinite, however. Systolic retraction, apparent fixation of the apex and even Broadbent's sign may occur without pericardial adhesions.

Cirrhosis of the liver is important in differential diagnosis. But it can readily be ruled out on the basis of the patient's history, the cardiovascular findings and the results of liver function studies.

*Prognosis.*—The prognosis is largely dependent on the state of the myocardium and the extent of the hepatic involvement. The patient may live for years with extensive adhesions but is often an invalid. Death usually results from cardiac failure, recurring ascites or intercurrent infection.

*Treatment.*—For the minor varieties of adhesive pericarditis no treatment is indicated. At times the usual treatment for heart failure (rest, digitalis, low-sodium diet, mercurial diuretics) may help relieve most of the symptoms. However, when the adhesions interfere with cardiac filling or constrict the large vessels, surgery is the indicated treatment. Most surgery is done in the healed stage of tuberculous or septic pericarditis. When moderate or severe cardiac failure occurs and the mercurial diuretics and the regimen previously outlined fail to give relief, the Brauer operation is performed. This consists in the resection of the third to sixth ribs from the midclavicular to the anterior axillary line to give the heart more space. This is done most often in rheumatic heart disease when adhesions exist between the heart and the chest wall. Under those circumstances some improvement may follow the operation. The Delorme operation actually resects the pericardial adhesions from the heart and the inferior vena cava. Modifications of this type of surgery are being done today more and more frequently for the treatment of adhesive pericarditis. In doing the Delorme resection for pericarditis the major difficulty occurs when the adhesions are around the posterior surface of the heart. This

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particularly that associated with high grade anemia and thyrotoxicosis

The incidence is highest between ten and thirty years because of the prevalence of rheumatic heart disease during this period and rapidly recedes after forty years of age. This disease however persists to a limited extent in the upper age groups and is occasionally observed after sixty years. The arteriosclerotic type begins to appear at about fifty years and increases thereafter. The females predominate slightly in the rheumatic group, more particularly in cases with mitral stenosis.

*Pathology.*—Healing probably occurs in certain of the milder forms of acute endocarditis without any significant residual damage or perhaps no more than a slight thickening or contracture of the valve leaflets. When, however, the involvement is more extensive or there are repeated invasions of the valve structures from exacerbations or recurrence of the infection, the valvular deformity usually becomes a more prominent feature. The entire valve structure and often the mitral ring may be involved. In the more chronic cases there is fusion of the valve leaflets, shortening of the chordae tendineae and not infrequently an extensive calcification. The valves are held in a partially open position. This frequently produces a rigid irregular or funnel shaped structure projecting into the cavity of the left ventricle with an opening varying in size and shape. There is thus produced a combined stenosis and insufficiency in which either effect may dominate. The higher grades of obstruction are designated as pure mitral stenosis. The opening may be represented by an irregular narrow slit or be oval in shape, possibly barely admitting the tip of the little finger. A pure mitral insufficiency is seen in the earlier stages of the disease before the valve structures become rigid and is therefore the prevailing mitral lesion in childhood. It is also observed at a later age when there is a limited deformity of the valves. The stenosis represents a more advanced stage in the development of the valve defect and may not appear for five or ten years or even for a longer period after the original valvulitis.

The additional alterations in the heart vary with the extent and character of the mechanical handicap and the associated involvement of the myocardium. If the valvular lesion is primarily a stenosis, an extra load is placed on the left auricle and right ventricle. There is at first a dilatation and hypertrophy of the left auricle. The capacity of the left auricle is normally under 50 cc. In the more advanced forms of obstruction it may be increased to 500 or even 700 cc. The projection of the dilated chamber posteriorly and to the left produces one of the most distinctive roentgenologic findings of mitral stenosis. The obstruction to the flow of the blood into the left ventricle leads to an increase in the pulmonary pressure which may finally result in pulmonary congestion, fibrosis and possibly a sclerosis of the pulmonary vessels. This in turn adds to the work of the right ventricle which is later manifested by a hypertrophy and dilatation. As the right ventricle increases in size it occupies more and more of the anterior surface of the heart and in the more advanced stage may for the most part make up the apex which is normally produced by the left ventricle. The left ventricle, under these circumstances, is not increased in size to any significant extent and may be actually smaller than normal. When, however, the mitral stenosis is associated with a distinct insufficiency, the left ventricle is involved along with the left auricle and the right ventricle. In general the heart is larger with a double lesion. The most extensive cardiac enlargement is seen in patients with rheumatic heart disease who die within a few years after the initial cardiac infection. An insufficiency is generally the outstanding lesion. The associated involvement of the myocardium, however, is a prominent factor. The insufficiency is thus produced not only by the deformity of the valve leaflets but by a dilatation of the mitral ring. While under these conditions the mitral insufficiency contributes to the cardiac disability, it is not as important as the damage to the myocardium.

MITRAL STENOSIS.—*Symptoms.*—The symptoms in general are not characteristic in mitral stenosis. They seldom appear

gives trouble because of the danger of the development of ectopic rhythms cardiac standstill, tear of the heart muscle, pneumothorax, and pneumonia

## CHRONIC VALVULAR HEART DISEASE

In certain forms of heart disease more especially in the rheumatic type the mechanical handicap imposed by an insufficiency or a stenosis or, more often a combination of these effects, from a deformity of the valve structures, is a prominent aspect or may even dominate the subsequent course This, however is not the only factor in the development of the cardiac disability The valve lesions are frequently progressive and in the more advanced stages particularly following rheumatic fever are generally dependent on repeated recurrences or exacerbations of the infection with an associated involvement of the myocardium The damage to the myocardium may thus be a significant feature of the disease and, in those who die within a few years following the initial infection usually overshadows the valve lesions

In arteriosclerotic heart disease the structural alterations in the myocardium are usually far more significant than the associated valvular defect The aortic insufficiency from a syphilitic involvement of the aorta is customarily mentioned in connection with aortic valve disease This, however, is primarily dependent on a dilatation of the aortic ring and the deformity of the valves

Statistics as to the relative frequency with which the different valves are concerned vary somewhat depending on the incidence of syphilis and whether the diagnosis is established clinically or by a postmortem In the figures cited by White including more than 3000 cases with two series totaling 508 cases in which the diagnosis was established at necropsy, the mitral valve was involved in 70 to 85 per cent, the aortic 42 to 45 per cent tricuspid 10 to 15 per cent and the pulmonic valve in approximately 1 per cent There was a surprisingly close agreement in the two series of necropsy cases The mitral valve was diseased alone in 50 to 60 per cent and the aortic in 10 to 20 per cent A tricuspid lesion is usually associated with an involvement of the mitral valve and seldom diagnosed clinically, except when manifested by an insufficiency Tricuspid insufficiency is relatively common, but usually results from a dilatation of the valve ring rather than from a deformity of the valve structures It is thus designated as a relative insufficiency The mitral valve ring is frequently concerned in the same manner In many instances, particularly when the patient *is first seen during cardiac failure* it may be difficult or even impossible to determine the extent to which a mitral insufficiency is dependent on a disease of the valve structure or a dilatation of the heart The distinction however, is frequently not of any great importance at this stage of the cardiac disability since it may have little or no bearing on the prognosis or treatment

### Mitral Valve Disease

*Etiology* —Mitral valve disease results from valvulitis in the vast majority of cases and rheumatic fever is by far the most important etiologic factor A mitral stenosis is generally regarded as being pathognomonic of a rheumatic infection The history, however is not infrequently negative for rheumatic fever more particularly in the latent form which occurs especially in women There still remains a group in which the nature of the infectious agent is unknown If however the cases with a varying degree of stenosis and those in which an arteriosclerosis is probably the responsible factor are excluded the remaining group is relatively small

A thickening and sclerosis of the valve structures occasionally result from an arteriosclerosis In rare instances an extensive calcification may involve the entire valve ring Under these conditions the possibility of a previous infection is difficult to exclude In most instances the mitral insufficiency associated with an arteriosclerosis is dependent upon myocardial changes and a subsequent dilatation of the auriculoventricular ring A relative insufficiency of the mitral valve also occurs in various other forms of myocardial weakness

position the posteriorly displaced left auricle will elevate the left bronchus In the right anterior oblique position one of the most distinctive *roentgenologic signs* of mitral stenosis is found It is best elicited by giving the patient a swallow of barium and observing the displacement of the esophagus posteriorly by the enlarged left auricle

There is not infrequently a right axis deviation in the *electrocardiogram* which in some instances may be quite marked The P wave is often more prominent the duration generally increased and the summit frequently notched Evidences of right ventricular hypertrophy will also develop in time The precordial leads over the right ventricle will show delay in onset of the intrinsicoid deflection as well as increased voltage of the R waves and inverted T waves Right bundle branch block may also be seen under these circumstances The findings are generally considerably altered by a significant mitral insufficiency There is invariably a more evident increase in the size of the heart In the more advanced forms the heart may be very large The apex impulse under these conditions is usually diffuse and often extends well out side the midclavicular line The displacement of the apex is more outward than downward The diastolic murmur is frequently not so prominent or perhaps only evident after exercise or excitement

*Complications* —The tremendous strain placed on the left auricle the increased tension in the pulmonary circulation and the added load on the right ventricle may produce a characteristic train of complications In the hypertrophy and dilatation of the left auricle a stage is frequently reached in which the auricles fail to contract in a normal fashion and an auricular fibrillation is established This may be preceded by a period of irregularity from premature contractions Mitral stenosis is one of the most common causes of auricular fibrillation The dilatation of the auricles also permits other possibilities In some cases the left auricle may enlarge to such an extent that its shadow roentgenographically is seen to be to the right of the cardiac shadow producing the so-called double contour on the right side of the heart This is known as "massive left auricle In the more advanced forms and particularly after the onset of the auricular fibrillation the rate of the blood flow within these dilated chambers is greatly reduced This not infrequently permits the blood to coagulate especially in the crevices in the auricular appendages Occasionally bits are dislodged pass into the circulation and go to the brain spleen kidneys mesenteric vessels or perhaps to the extremities In rare instances a ball thrombus is formed in the left auricle which may intermittently further obstruct the mitral orifice and produce distressing attacks of dyspnea and precordial discomfort

The increased tension in the pulmonary circulation is prone to produce pulmonary congestion This along with the increased susceptibility to respiratory infections may lead to blood tinged sputum occasionally a frank hemoptysis and in certain instances findings very suggestive of pulmonary tuberculosis This increased pulmonary pressure may also lead to pulmonary arteriolosclerosis which will throw a further strain on the right heart The failure of the right ventricle is evidenced by a relative tricuspid insufficiency and an engorgement of the liver A prolonged engorgement of the liver may ultimately terminate in cirrhosis and portal obstruction In certain instances the hepatic complications may be an important feature in a later stage of the disease

*Diagnosis* —A mitral stenosis is ordinarily recognized by the thrill and characteristic murmur In the early stages of the lesion however the murmur may be readily over looked It may not be present at rest and perhaps brought out only by exercise or amyl nitrite The murmur is usually heard best in the recumbent position and frequently made more evident by turning the patient on the left side which brings the heart more in contact with the chest wall It should be remembered that after the onset of the auricular fibrillation the presystolic phase of the murmur generally disappears A short early diastolic murmur with possibly a snappy first sound may be the only auscultatory findings An apical diastolic murmur (the Austin Flint murmur) of the same general character may be associated with an aortic insufficiency The aortic lesion is

until there is an extensive impairment in the cardiac function and usually represent a beginning failure of the myocardium. Certain complications may, however, occur before the onset of the more evident signs of cardiac failure. Precordial pain or ache may be noted. In some the pulmonary congestion and possibly an associated respiratory infection is productive of blood tinged sputum or even a frank hemoptysis. A cerebral accident or splenic infarct is occasionally the first manifestation of a mitral stenosis. In other cases the attention is perhaps first directed to the heart because of premature contractions, possibly paroxysms of auricular fibrillation, or more often the onset of shortness of breath.

*Physical Findings.*—The findings prior to the onset of the cardiac failure, except for certain complications as mentioned above, are confined to the heart. The information obtained by inspection is not infrequently surprisingly negative. In some, particularly in thin chested individuals, the apex impulse may be rather prominent and of a diffuse character. It frequently does not extend beyond the midclavicular line. Occasionally abnormal pulsations are noted in the third and fourth left intercostal spaces from an overactive pulmonary artery. The presystolic thrill is one of the most distinctive signs of mitral stenosis. It is often confined to a small area usually well within the outer border of the apex impulse and corresponds with the location of the murmur. In the beginning the thrill is only felt with an accelerated heart rate. It is crescendo in character and terminates abruptly with the first heart sound which is often manifested by a sudden shock. There is likewise a diastolic shock over the pulmonic area. Occasionally, particularly in the more advanced forms, the thrill may be divided into two stages, the decrescendo and the crescendo, corresponding to the two phases of the murmur. On percussion there is often no significant increase in the size of the heart. An extension of the dullness to the right of the sternum may be demonstrated but this is often difficult to elicit until the onset of cardiac failure and a more extensive dilatation of the right auricle. The heart is likely to be globular in shape chiefly because of the filling out in the region of the left auricle and pulmonary artery.

The passing of the blood from the left auricle to the left ventricle through the constricted and irregular opening sets up a vibration which is not only responsible for the diastolic thrill but also the diastolic murmur. The latter is another distinctive finding in mitral stenosis. The murmur and the thrill, as well, obviously correspond with the particular period during the diastole in which the velocity of the blood passing from the left auricle to the left ventricle is greatest. It therefore first appears in late diastole during the period of the auricular contraction and ends abruptly with a snappy first sound. Later, as the obstruction progresses, it advances toward the mid-diastolic period and finally an early diastolic murmur is heard. The murmur may occasionally extend throughout the diastolic period with perhaps a reduction in the intensity in the mid section. With the onset of an auricular fibrillation the presystolic phase of the murmur usually disappears and only that occurring during the first half of the diastole is heard. If, however, the cardiac rate is accelerated the murmur may again take on a presystolic aspect because of the shortening of the diastolic period. It is at times necessary not only to exercise the patient but also to listen at his mitral area with the patient in the left lateral recumbent position to elicit this presystolic murmur. The snappy first sound is a prominent feature and in certain instances may not be preceded by a murmur. An accentuation of the pulmonic second sound is generally very evident and not infrequently there is a reduplication. The amplitude of the radial pulse may be reduced but the tension is fairly well maintained. There may be some reduction in the systolic blood pressure.

The findings from the roentgenologic examination are often helpful in the diagnosis of mitral stenosis. The globular shape of the heart from the filling out in the region of the left auricle and the pulmonary artery is suggestive. This produces a straightening of the left border of the heart. The dilated left auricle projects posteriorly and slightly to the left. In the left anterior oblique

murmur The lesion continues to be an insufficiency until through the subsequent healing and perhaps recurring damage, the valves are further deformed and their movement greatly restricted This may require three to five or even ten years and then the evidence of a stenosis appears In certain instances however especially when there is a limited damage to the valve the lesion continues as an insufficiency Mitral insufficiency in later life may be produced by thickening or curling of the edges of the valve leaflets or a shortening of the chordæ tendineæ from an arteriosclerosis It is however, more often a relative insufficiency produced by a cardiac dilatation

*Physical Findings* —There is a remarkable variation in the size of the heart with this lesion depending on the stage and the extent of the myocardial involvement The character and location of the apex impulse is one of the most reliable guides in estimating the extent of the cardiac enlargement If it is forceful and displaced to or beyond the mid-clavicular line it is generally safe to conclude that the heart is enlarged In the more advanced stages there is frequently an extensive cardiac dilatation and hypertrophy involving both the right and left chambers The precordium under these circumstances is usually prominent and there is frequently a widespread pulsation extending from the left border of the sternum to or even well beyond the anterior axillary line The more definite apex impulse is usually located in the fifth or sixth interspaces The contraction of the heart is forcible and possibly lifts the entire left lower anterior chest The second sound especially over the pulmonic area may be readily felt In the early stages of the cardiac enlargement the dullness is only increased to the left Later as the dilatation and hypertrophy progress there is an evident general enlargement of the heart as indicated by an extension of the dullness both to the right and to the left The murmur is systolic in time and soft blowing harsh or even musical in character It replaces partly or entirely the first sound and may be heard over the entire precordium The transmission is to the left toward the axilla and possibly backward to the angle of the scapula There is usually an accentuation of the second pulmonic sound

*Diagnosis* —The diagnosis is usually evident but may be very difficult It is at once apparent when there is a cardiac enlargement and a systolic apical murmur transmitted to the left The recognition is by far the most important during the acute stage of the valvulitis At this time the murmur is generally soft blowing in character and possibly not transmitted to any significant extent The apical region is furthermore a very common site for systolic murmurs not dependent on an organic basis Some are definitely of the cardio respiratory type The explanation in certain instances however is not clearly understood Systolic murmurs are likewise encountered over the pulmonic area and may be heard well toward the apex These physiologic murmurs are not infrequently mistaken for a mitral insufficiency The diagnosis may be extremely difficult when a child is seen for the first time particularly during an acute infection The character of the infection past history and possibly evidence of rheumatic fever are important The size of the heart however is a deciding factor In questionable cases the appearance of even a faint presystolic rumble at a later period in the development of the valve lesion establishes the significance of the systolic murmur Theoretically the endocardial type of insufficiency should be associated with a certain degree of stenosis Generally these lesions are combined to such an extent that both effects may be recognized In the mitral insufficiency that appears in later life it is often impossible to differentiate between that due to a deformity and that resulting from cardiac dilatation The history and findings relative to the blood pressure the condition of the arteries the myocardium and the possibility of an anemia and thyrotoxicosis are helpful in the diagnosis

*Prognosis* —The prognosis is largely determined by the condition of the myocardium The outlook in children is always in doubt because of the possible recurrence of rheumatic fever and the extension of myocardial damage It is unfortunately poor in those with an extensive cardiac enlargement

identified by the enlargement of the left ventricle and the peripheral vascular phenomena When, however there is a combined aortic and mitral lesion, particularly the rheumatic type, it is frequently difficult, or even impossible, to differentiate between the Flint murmur and that of a mitral stenosis In the aortic insufficiency from a syphilitic aortitis, it is generally safe to assume that there is not a mitral stenosis The faint diastolic murmur to the left of the sternum from pulmonary insufficiency, may be mistaken for an aortic insufficiency The absence of the other signs of an aortic lesion is generally sufficient to exclude the possibility

An apical diastolic vibration is not infrequently observed in the overactive heart of hypersensitive individuals, occasionally heard in the cardiac enlargement involving the left ventricle especially with an adherent pericardium The history and associated findings usually permit a differentiation

*Prognosis* —Mitral stenosis represents one of the most serious forms of chronic valvular heart disease because of the progressive nature of the lesion and the possibility of grave complications The prognosis in general is dependent on the extent of the stenosis, the age of the individual and associated damage to the myocardium The outlook is usually poor in a relatively young individual and the majority die before the age of forty years Isolated instances of fairly high grade stenosis are observed after fifty or even sixty years of age In 100 patients studied clinically and pathologically (Stone and Feil) the average age of death of males was 42 7 years, and of the females 38 6 years Eighty-one of these people were admitted to the hospital because of congestive failure The duration of life from the onset of cardiac failure varied greatly, but averaged 3 5 years Auricular fibrillation was present in 50 of the 94 cases in which the cardiac mechanism was definitely known Of the 46 patients with embolic manifestations, 30 (65 per cent) had auricular fibrillation Subacute bacterial endocarditis is relatively uncommon in high-grade mitral stenosis and rarely observed in the presence of auricular fibrillation In general pregnancy is well tolerated but is not advisable when there is significant reduction in cardiac function and particularly if there are signs of approaching cardiac failure Occasionally there is a history of repeated pregnancies without any impairment in the cardiac function The incidence of intercurrent infection possibly recurrent damage to the myocardium, and the social and economic status of the individual are very important factors If the individual carefully conserves the cardiac function and is fortunate in escaping complications the onset of the cardiac failure may be postponed for years and death may possibly result from some other condition

*Treatment* —Recently, several surgical approaches have been developed for the treatment of mitral stenosis The exact indications for surgery are not yet entirely clear It is generally felt however, that the patient with tight mitral stenosis and frequent bouts of left-heart failure who has no or only slight left ventricular enlargement is the ideal case Valvulotomy of the posterior mitral valve has been done but leads to much regurgitation Commissurotomy because of its more physiologic approach, has become more popular of late and is at this time the operation of choice A shunt operation in which the pulmonary vein is hooked up with the azygous vein has also been performed with some degree of success Auricular fibrillation contraindicates surgery At present the operative mortality rate for the commissurotomy is about 10 per cent

Amputation of the auricular appendage has been done in some cases of peripheral embolization This is a comparatively simple and safe operation

MITRAL INSUFFICIENCY —Mitral insufficiency was at one time considered to be the most frequent form of valvular heart disease If however the term is restricted to the insufficiency that is dependent on the deformity of the valve structures and the cases with recognizable stenosis are excluded it is not a very common lesion Mitral insufficiency is the earliest manifestation of an acute valvulitis In the beginning particularly in the rheumatic type the dilatation of the mitral ring from the associated involvement of the myocardium is an important factor in the production of the

should always include the determination of the etiologic factor along with the estimation of the extent of the impairment in the cardiac function

*Prognosis* —The prognosis is determined by the extent of the insufficiency the etiologic factor the presence of other valve defects and the state of the myocardium An aortic insufficiency of the rheumatic variety may be borne for years without much impairment in the cardiac function Here again there is ever the possibility of a recurrence of the rheumatic fever with a further increase in the valvular deformity, new insults to the myocardium and perhaps the involvement of other valves The outlook in the syphilitic form is usually poor The changes in the aorta are generally advanced by the time the insufficiency is discovered and the course is frequently steadily downward There is seldom an extensive regurgitation in the arteriosclerotic variety but there is likely to be a significant involvement of the coronary arteries A moderate stenosis, both in the rheumatic and arteriosclerotic forms limits the extent of the insufficiency and thereby leads to a more favorable prognosis If however the lesion is associated with an involvement of the mitral valve, a greater handicap is placed on the heart

Aortic Stenosis —An advanced aortic rheumatic valvulitis or sclerotic changes in the valves However it is frequently not recognized until the later years of life Other valves particularly the mitral, are often involved The aortic lesion usually produces a combined insufficiency and stenosis but not infrequently it may be difficult to hear a diastolic murmur

Calcific aortic stenosis may also be seen The exact etiology of this condition is not known it is often on a rheumatic basis

The left ventricle is obliged to work against an increased resistance In the early stages the change in the left ventricle is manifested chiefly by hypertrophy The wall of the left ventricle is therefore often greatly thickened without much increase in the size of the left ventricular chamber The systolic phase of the heart is prolonged in order to compensate for the obstruction to the passage of the blood into the aorta This accounts for the well-sustained pulse tension noted in aortic stenosis With the gradual impairment in the function of the left ventricle dilatation is more evident and the left auricle and finally the right ventricle are involved

*Symptoms* —There are ordinarily no symptoms until shortly before the onset of cardiac failure Dizziness or fainting attacks from a cerebral anemia are not infrequently the first manifestations These attacks of dizziness and fainting are just as often the result of vagal reflexes with increase in vagal tone These symptoms usually occur with exertion and are often associated with some shortness of breath Substernal pressure or true anginal pain may be experienced The anginal symptoms however, are not so frequent as in aortic insufficiency

*Physical Findings* —The cardiac enlargement is readily elicited in the younger subjects but may be masked in the elderly individuals by an emphysema The apex impulse is usually not a conspicuous feature or perhaps the location is determined only by careful palpation The attention is usually attracted at once by the rough grating or musical murmur over the aortic area communicated to the suprasternal notch and to the vessels of the neck The aortic second sound is seldom heard In rare instances particularly in the advanced form after the onset of cardiac failure the murmur may be barely audible or perhaps entirely absent The intensity of the murmur under these circumstances increases with the improvement in cardiac function There is often a faint diastolic murmur and a musical systolic murmur is rather common at the apex A thrill accompanies the harsh aortic murmur and is likewise transmitted to the upper sternum and vessels of the neck This thrill varies with the intensity of the murmur and in certain instance may be barely palpable or possibly not elicited It may be brought out by having the patient lie on his anterior chest over a firm surface The absence of a thrill does not preclude the diagnosis

The change in the pulse is one of the most distinctive features It rises very slowly and is well sustained producing in the sphygmo

the explanation usually given it is assumed that the regurgitant blood stream from the aorta holds the anterior cusp of the mitral valve in the way of the blood passing from the left auricle into the left ventricle, and thus produces a relative mitral stenosis. A *similar murmur, however, may occur in a* large heart without aortic insufficiency. White has suggested that the dilatation of the left ventricle may be sufficient, with a relatively normal-sized mitral opening, to *permit the formation of a murmur, i e*, a relative stenosis.

The sudden increase and the abrupt fall in the arterial tension produces characteristic *vascular phenomena*. These features vary with the extent of the regurgitation and may thus be difficult to elicit in the early stages of the insufficiency or are made less conspicuous by an aortic or mitral stenosis. With a free aortic insufficiency there is generally extensive pulsation of all the peripheral arteries which is particularly noted in the neck and arms. In the advanced form, especially when there is an associated anemia, the head may nod and and perhaps the bed shake with each cardiac contraction. A pulsation of the retinal arteries is revealed by the ophthalmoscope. The capillary pulse may be demonstrated by slight pressure on the tip of the finger nail, by means of a glass slide on the lower lip, or by a gentle stroke across the forehead. This is manifested by a flush projecting into the zone of pallor with each cardiac contraction. The pulse is characteristically collapsing ("water hammer"—Corrigan). There is a sudden increase in the tension and an abrupt fall which is accentuated by slightly elevating the arm. This is reflected *in the blood pressure by* the abrupt increase in the systolic and a significant reduction in the diastolic phase. In the advanced stage it may not be possible to obtain a true diastolic reading. This produces an unusually large pulse pressure which in the extreme form is not observed in any other condition. Certain additional findings are encountered in the further examination of the peripheral arteries. If a brachial or a femoral artery is auscultated, it is noted that the abrupt distention of the vessel with each cardiac contraction is accompanied by a sound or even a sudden snap, the "pistol shot" sound. On compressing the vessel by the bell of the stethoscope, a point is reached when a diastolic murmur is heard, which is generally designated as the Duroziez sign.

The *roentgenologic examination* gives important information relative to the size and configuration of the heart but more particularly the condition of the aorta. It is indicated in every case where there is any *reason to suspect the possibility of a syphilitic* etiology and is not infrequently desirable in the arteriosclerotic form. The *electrocardiogram frequently* shows a left axis deviation. Changes in the *T* deflection and alterations in the *QRS* group, however, are more significant from the standpoint of the condition of the myocardium. One also usually finds the so-called left ventricular hypertrophy in the electrocardiogram.

*Diagnosis.*—The diagnosis of an aortic insufficiency is ordinarily established without difficulty by the nature and location of the apex impulse, the general configuration of cardiac enlargement, the character and distribution of the diastolic murmur and the peripheral arterial phenomena. An aortic insufficiency is not infrequently overlooked because the diastolic murmur is not detected. The Flint murmur may be confused with the presystolic murmur of mitral stenosis. The absence of the usual accentuation of the first mitral sound and the association with an early diastolic murmur along the left border of the sternum and other manifestations of an aortic insufficiency, usually identify the condition. In rare instances a faint diastolic murmur (Graham Steell murmur) from a pulmonary insufficiency occurs. This, however, is invariably dependent on a high grade mitral stenosis which is usually apparent. In doubtful cases the diagnosis is based on the absence of peripheral vascular phenomena and roentgenologic findings with reference to the left auricle and the prominence of the pulmonary artery. The electrocardiographic findings may be helpful. In mitral stenosis a right axis deviation curve is usually encountered, whereas in aortic insufficiency a left axis deviation is more likely to occur. The diagnosis of an aortic insufficiency

differentiated from those transmitted from the aorta or right ventricle by palpating the edge of the liver between the two hands, or in thin subjects between the thumb and forefinger

The area of cardiac dullness is generally increased both to the right and to the left. There are frequently widespread precordial pulsations which may be particularly forceful over the lower sternum from the heaving contraction of the right ventricle. Various murmurs are heard depending on the associated valvular involvement. A tricuspid insufficiency produces a systolic murmur with maximum intensity over the lower sternum. With a relative insufficiency the murmur is usually soft blowing in character and limited in its distribution. In those in which the insufficiency is of valvular origin and generally associated with some degree of stenosis the murmur is more harsh or even rough in quality, transmitted to the right possibly in some instances as far as the anterior axillary line. Edema is usually present particularly with the relative insufficiency, and a generalized anasarca often develops. Occasionally the edema in the legs may disappear and the ascites persist. This is due to the development of a portal obstruction from prolonged engorgement of the liver.

*Diagnosis.*—The diagnosis in the early stages is generally not possible except by means of the polygraph. The location and the transmission of the murmur may suggest a tricuspid insufficiency but the diagnosis is finally dependent on the demonstration of a systolic pulsation of the veins. In a more advanced form this is very apparent in the veins of the neck or arms or is readily elicited by palpating the liver.

TRICUSPID STENOSIS.—Tricuspid stenosis is very rare and is usually associated with mitral stenosis. Cyanosis to a moderate degree may be present for years and rapidly progresses with the onset of cardiac failure. Shortness of breath is the most frequent complaint and generally easily induced.

The venous congestion with a cyanosis of the lips, nose, ears and hands and the engorgement of the jugular veins is a conspicuous feature. The cardiac findings are often masked by the mitral lesion. If however, the stethoscope is moved from the apex toward the sternum there are frequently two points of maximum intensity, one over the mitral valve area and the other over the tricuspid area. The cyanosis and venous congestion, a decided extension of the cardiac dullness to the right from a dilated right auricle, a harsh murmur over the lower sternal region and the early enlargement of the liver with presystolic expansile pulsation warrant a serious consideration of tricuspid stenosis. The use of the polygraph is important in establishing a diagnosis. A faint pulsation of the jugular veins is normally produced by the contraction of the right auricle. In tricuspid stenosis with sinus rhythm this is markedly increased and constitutes one of the most distinctive signs. Occasionally, as pointed out by Friedlander and Kerr (1936) this wave is sufficiently exaggerated to permit detection without the aid of instruments through the combined inspection of the apex beat and the jugular pulse.

### PULMONARY VALVE DISEASE

Lesions of the pulmonary valves, aside from congenital anomalies, are exceedingly uncommon. These valves are rarely invaded by rheumatic infection. In a series of 97 cases reported by Coombs, the pulmonary valves were involved in only 2 instances. Rare instances are recorded in which damage has resulted from various types of infections. Sclerotic changes are occasionally encountered and an involvement by subacute bacterial infection has been reported. A stenosis or insufficiency may presumably result from these various causes but they are exceptional occurrences. When a pulmonary stenosis occurs it is almost invariably from a congenital anomaly. The signs of this lesion are considered under congenital heart disease.

Systolic murmurs are extremely common in the pulmonary region. They are usually soft blowing in character, occasionally have a harsh quality and are seldom transmitted to any significant extent. These murmurs are more particularly seen in children and thin-chested individuals, occur with fever, and are commonly observed in anemic

graphic tracing the characteristic broad plateau like peak. The systolic blood pressure is frequently low and possibly not more than 90 to 100, with a diastolic pressure at about the normal level. This gives a small pulse pressure, ranging between 15 and 25 mm Hg. The character of the pulse and blood pressure readings is altered by the extent of the insufficiency. The electrocardiogram usually shows a marked left axis deviation. An inversion of the *T* wave and alteration in the *QRS* group are common, particularly in the arteriosclerotic form.

*Diagnosis*.—The diagnosis is based on the murmur, thrill and character of the pulse. The pulse is by all means the most distinctive finding. Systolic murmurs are common over the aortic area in hypertension, syphilitic aortitis and subacute bacterial endocarditis without a significant stenosis. Moreover, the presence of a thrill is not necessarily indicative of a stenosis. The diagnosis of aortic stenosis therefore is justified only when the murmur and perhaps a thrill, are associated with characteristic change in the pulse. If however the rough murmur over the aortic area transmitted to the vessels of the neck is associated with a mitral lesion and particularly if there is a history of rheumatic fever, the possibility of an aortic stenosis should be seriously considered. In certain instances it is possible that aortic stenosis may be confused with pulmonary stenosis. In the latter however, the murmur and thrill are transmitted slightly to the left and not to the vessels of the neck and the characteristic alteration in the pulse is lacking.

*Prognosis*.—An aortic stenosis may permit many years of active life. At the onset of failure, however, the course is usually downward. The arteriosclerotic form is not infrequently a late development. It may not necessarily reduce the life expectancy. Some have been known to live to ripe old age. Those with rheumatic aortic stenosis however, usually die between 30 and 40 years of age.

*Treatment*.—Surgery for stenosis of the aortic valve is performed but is still experimental.

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The tricuspid valves are occasionally involved in a rheumatic infection. The necropsy findings reported by Coombs would seem to indicate that the incidence is fairly high in the more extensively damaged hearts. In 97 cases these valves were concerned in 35. In every instance there was an associated involvement of other valves, more particularly the mitral valve. These lesions, however, seldom result in a significant insufficiency and stenosis. While a tricuspid insufficiency is relatively common, it is generally due to a stretching of the auriculo ventricular ring from a dilatation of the right ventricle. A stenosis is rarely encountered and not usually diagnosed during life.

Tricuspid Insufficiency.—This condition may occur from a valvular deformity but generally results from a dilatation of the right ventricle (relative insufficiency). The relative insufficiency therefore is usually associated with congestive failure.

*Physical Signs*.—The transmission of a systolic pulsation to the veins of the neck, the upper extremities and particularly to the liver through the regurgitation of the blood from the right ventricle to the right auricle is one of the most distinctive signs. The pulsation in the neck is usually more evident in the right supraclavicular triangle lateral to the sterno-cleido mastoid muscle where the external and internal jugulars enter the subclavian vein. It is synchronous with the carotid pulse but may be distinguished from the latter by pushing the vein to one side or in doubtful cases by a polygraphic tracing. In the more advanced form the pulsation may be detected by gently palpating the external jugular vein between the thumb and forefinger. This phenomenon is frequently observed in the most characteristic form in the arms. It is brought out by slowly raising the arm to a point just preceding the collapse of the vein. Occasionally the pulsation may be observed in the veins of the shoulders and chest. The regurgitation of the blood in the inferior vena cava and the hepatic vein produces a systolic pulsation of the liver. This is expansile in character and may be

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## MYOCARDITIS

There are two kinds of myocarditis one is characterized by a true inflammatory reaction in the cardiac musculature the other by a primary degeneration of the cardiac musculature from toxins viruses or other factors with a secondary inflammatory change (which may be reparative)

*Pathology* —The gross appearance of the heart varies with the extent of myocardial damage In the more extensive form the muscle is soft and flabby and frequently presents a mottled appearance Occasionally minute epicardial hemorrhages are seen There is generally a diffuse parenchymatous degeneration involving especially the ventricles In the microscopic examination varying stages of degeneration are encountered In the beginning muscle fibers stain light pink and the cross striations are indistinct Adjoining sections of the myocardium may show areas with extensive degeneration with an albuminous exudate and infiltration of polymorphonuclear and mononuclear cells between the diseased muscle strands An advanced form of degeneration with areas of necrosis is seen in diphtheria In the myocarditis associated with septicemia bacterial emboli may lodge in the smaller arterioles and produce an abscess The more chronic varieties of myocarditis show various stages of healing with connective tissue proliferation

*Etiology* —Myocarditis is usually found in association with infections such as diphtheria scarlet fever pneumonia septicemia pyemia bacteremia typhoid fever paratyphoid fever dysentery measles mumps influenza (particularly influenza A virus) meningitis poliomyelitis rickettsial disease (especially scrub typhus) helminthic diseases (trichinosis) and trypanosomiasis Nephritis and sensitivity to drugs (arsphenamine bismuth sulfonamides emetines etc ) may also cause myocarditis

In addition to myocarditis of known etiology there are types of the disease that are idiopathic or primary *e g* congenital myocarditis and Fiedler s isolated myocarditis

*Symptoms and Signs* —Since myocarditis is often a terminal condition it may be overshadowed by the symptoms of the primary condition Myocarditis should be suspected when there is a marked discrepancy between pulse rate and temperature Furthermore a sudden fall in arterial blood pressure even if slight may indicate myocarditis as may dyspnea and cyanosis in a patient who has not exhibited these signs before Sudden marked weakness or collapse after slight exertion sometimes ushers in the condition sometimes increased irritability upper abdominal discomfort with nausea and vomiting from distention of the liver are early symptoms There may also be a change in the quality of the cardiac sounds possibly the development of a gallop rhythm Furthermore a faint systolic apical murmur may appear The accelerated rate may suddenly drop when there is an onset of heart block In some cases the patient may die very suddenly without any other previous symptom In cases of so-called primary myocarditis the clinical course is very short It is a fulminating disease characterized by respiratory distress arrhythmia elevated temperature slow pulse rate and unexpected death

*Electrocardiographic Changes* —The electrocardiogram affords valuable means of following the course of the myocardial involvement In the advanced stages of myocarditis the curves frequently show varying degrees of auriculoventricular heart block alterations in the *QRS* complexes various types of premature contractions, and occasionally, auricular fibrillation In addition to the slurring and widening of the *QRS* complexes changes in the *T* waves may also be found Though these changes are similar to those seen in myocardial infarction they differ in that the *Q* waves of myocardial infarction are not seen and the usual sequence of the myocardial infarction picture does not occur

*Diagnosis* —In patients with any of the infections mentioned above *and* heart signs the diagnosis is usually clear and is confirmed by the electrocardiographic findings

*Prognosis* —For cases of Fiedler s myocarditis the prognosis is usually very poor death occurring rapidly In other cases the prognosis depends on how much of the myocardium is involved and the body s ability

states They are often altered by posture and frequently influenced by respiration Occasionally a systolic murmur of a mitral insufficiency may be transmitted to the pulmonary region These functional or physiologic murmurs are distinguished by their *location and character, the influence of* posture and respiration, and the fact that they are not associated with demonstrable structural changes in the heart The diagnosis may be established by the methods described under congenital pulmonary stenosis

An *insufficiency of the pulmonary valve* is generally functional and usually associated with a high grade mitral stenosis Occasionally this may result from supernumerary cusps of the pulmonary valve (Kissin, 1936) It is manifested by a soft diastolic murmur (Graham Steell murmur) along the left border of the sternum This murmur is strikingly similar to the diastolic murmur of aortic insufficiency It is distinguished from the latter only by the absence of the vascular phenomena and by the associated findings of a mitral stenosis The differentiation in certain instances may be extremely difficult and perhaps not established until after a period of observation In most instances in which a pulmonary insufficiency is suspected the murmur is finally proved to be that of an aortic insufficiency

*Treatment of Pulmonary Stenosis* —At present there are three types of operative procedure for the relief of pulmonary stenosis In the Blalock-Taussig shunt operation an end to side anastomosis is made between the subclavian artery and one of the branches of the pulmonary artery This is best done in patients who are from 3 to 10 years of age The mortality rate for this operation is about 10 per cent

Another shunt operation is that of Potts He anastomoses the aorta to the left pulmonary artery with a special clamp This procedure is best in patients past twenty years of age With it, one can control the size of the shunt

Brock has attacked the stenotic pulmonary valves themselves In his operation a valvulotomy is done *to permit free flow* of blood through the stenotic area

These operations have been most effective in relieving the load on the right heart as well as increasing oxygenation of the blood

*Medical Treatment of Chronic Valvular Heart Disease* —These patients should be under the general supervision of a physician When first seen the infection and other factors which may promote the cardiac disability should as far as possible be removed The treatment therefore is largely a matter of protecting the subject against further cardiac insults and overtaxing the heart by physical strain This form of heart disease frequently progresses through the return or an exacerbation of the rheumatic infection It is therefore important that more than the usual precaution be taken against infection particularly of the upper respiratory tract and the individual confined to bed during the active stage of the infection or until the physician is certain that the heart is not damaged Reinfections of the heart are usually too often not recognized and thus protective measures are not instituted Excessive physical strain more especially with a mitral stenosis or an aortic insufficiency often contributes to a reduction in the functional capacity of the heart The physical activities under these circumstances demand careful consideration and adjustments are not infrequently necessary With the more serious forms of valvular lesions as a mitral stenosis or an aortic insufficiency competitive athletics are prohibited If the cardiac lesion is discovered in childhood the child should be encouraged to continue in school in order that he may be able to gain a livelihood without resorting to physical labor In women the advisability of pregnancy at times comes up for consideration Many with a moderate degree of mitral stenosis go through pregnancies without any apparent ill effect With a marked aortic insufficiency or a high grade mitral stenosis there is a likelihood of trouble and with an evident reduction in the cardiac function pregnancy should always be avoided or if it occurs terminated at an early date The individual's great desire for a child may in certain instances justify chances that would otherwise not be taken (*See* page 852 )

findings will be accentuated by placing the patient under any type of stress Blood pressure is normal in most cases as are resting circulatory measurements and cardiac output The heart size is normal And the electrocardiograms are usually normal however they may occasionally show inverted *T* waves in Lead II The patients also show an abnormal reaction to pain Pulmonary ventilation is abnormal The blood lactate level is abnormally high after standard effort on the patient s part

*Prognosis* —The prognosis in the so-called acute case is much better than in the chronic In all cases prognosis as to life is good the prognosis as to immediate re covery from any given episode depends upon the condition of the patient and the therapy used The severity of the condition is thought to be greater and the prognosis relatively poorer in military than in civilian life

*Differential Diagnosis* —Neurocirculatory asthenia must be differentiated from true heart disease thyrotoxicosis and psychoneu rosis *per se* These diseases may be ruled out by use of the appropriate tests (*see* Chapters 16 and 31)

The most difficult differentiation is between true neurocirculatory asthenia and psychoneurosis especially of the anxiety type for one is often engrafted upon the other Many cases of psychoneurosis have cardiac manifestations as the outstanding symptoms A recent history of nervous strain or infectious disease in a patient with a sensitive nervous system plus a history of hereditary background will establish the diagnosis of neurocirculatory asthenia

*Complications* —No particular complica tions have been found but the condition may precipitate a psychoneurosis

*Treatment* —The treatment in every case depends on the cause, but rest is the important therapy The patient may need months of rest and quiet The period of rest com pleted rehabilitation re-education and retraining should follow Reassurance of the patient is most important in a few cases psychotherapy is necessary The fewer examinations done once the diagnosis has been established the better It is of prime importance to dispel any fears as to the possibility of heart disease or imminent death Accurate diagnosis is essential no careless diagnosis of myocarditis or cardiac insufficiency should ever be made Nor should the patient be told that he has only imaginary disease The patient requires the complete sympathy of the physician and the assurance that the physician does not consider him a malingerer The patient also requires a careful plan for day to-day living He must avoid late hours coffee tea overindulgence in alcohol and tobacco, and excitement Exhaustion and sudden strain must particularly be avoided

## SYNCOPE OF CARDIOVASCULAR ORIGIN

Syncope is due to cerebral anoxia cerebral anoxia may be due to brain disease heart disease postural effects or extrinsic factors

Syncope occurs in three stages depending on suddenness of onset and duration of the cerebral ischemia At first there is dizzi ness, the patient feels lightheaded sees spots before his eyes and feels faint In the second stage there is fainting due to cerebral anoxia It lasts only a few seconds In the third stage there is convulsive seizure occuring when the anoxia lasts more than from 9 to 15 seconds This convulsive seizure is a protective homeostatic mechanism to increase the blood supply to the vital centers

In syncope of cardiac origin we must first consider diseases of the *sinoauricular node* This node may be involved reflexly or it may be affected by arteriosclerosis coronary-artery occlusion acute infections myocarditis, or toxic factors When the sinoauricular node fails to function the auriculoven tricular node usually takes over as pacemaker of the heart But during this interval syncope may occur It must be pointed out however that the chief cause of sinoauricular nodal failure is an overactive vagal tone *Disease* of the *auriculoventricular node* may result in auriculoventricular heart block Syncope may occur during the transition from partial to complete heart block as well as during the continuance of complete heart block. At those times so-called Stokes-Adams seizures may occur *Ectopic rhythms* with rapid rates may result

to overcome the infection underlying the myocarditis Since the introduction of the newer antibiotics the prognosis in myocarditis is better

*Treatment* —Treatment of myocarditis is essentially a matter of protecting the heart in every way possible and overcoming the underlying infection The infection should be treated vigorously with any antibiotics that prove effective With the advent of penicillin streptomycin, aureomycin, chloromycetin, and terramycin in addition to the sulfonamides one may now quickly arrest many of the diseases which produce myocarditis It behooves us, then to isolate the offending organism as soon as possible and test it for sensitivity against all these powerful agents Then one should use adequate doses of any one or any combination of antibiotics The patient should be kept in bed and given adequate relaxation, every effort should be made to conserve the cardiac function through reduction in the cardiac load The diet should be simple and easily digestible Sedatives may prove very helpful Though it is sometimes necessary to use digitalis the patient s response is usually not satisfactory An icebag put on the chest may add to the comfort of the patient The patient should be kept in bed until all evidences of infection subside and the cardiac rate returns to a normal level The disappearance of the gallop rhythm and regression of cardiac enlargement are useful signs in judging the patient s progress An electrocardiogram may help the physician decide when to let the patient get up It is always advisable to keep myocarditis patients in bed longer than it seems necessary

NEUROCIRCULATORY ASTHENIA (Effort Syndrome DaCosta s Syndrome, Irritable Heart, Vasomotor Instability Cardiac *Neurosis*)

*Definition* —Neurocirculatory asthenia is characterized by nervousness easy fatigue subjective dyspnea, palpitation precordial pain faintness giddiness apprehensiveness poor performance of muscular work emotional stress headache, sweating, and tremor These symptoms are aggravated by effort or excitement and often follow infections or physical or nervous strain There is no diagnosable disease of heart, lungs, nervous system, or thyroid

*Etiology* —The cause of neurocirculatory asthenia is not known Heredity seems to play a major role in the etiology of this condition, as do malnutrition and overindulgence in tobacco, alcohol tea, or coffee

*Age* —Neurocirculatory asthenia is commonest in young adults, it is rare in young children It tends to increase after early adult life More than half the victims are between 20 and 40 Women are more often affected than men (6 to 4 ratio)

*Pathological Physiology* —No known organic pathological changes are present There are alterations, however, in the patient s physiologic response to effort There is little stamina for hard work, and there is a defect in aerobic metabolism when work is engaged in This is evidenced by oxygen consumption studies and blood lactate concentration Pulmonary ventilation is abnormal during work, as is ventilatory efficiency

*Symptoms* —(*see* definition) —The palpitation usually consists of a consciousness of forceful action of the heart which is sometimes rapid and usually regular, though occasionally extrasystoles may be present The precordial pain is usually a dull or heavy ache in the left breast It lasts for hours and does not radiate When the pain is severe it may radiate to the left arm and may be mistaken for angina pectoris This is believed to result from the type of respiration employed by these patients they use the diaphragm to a minimal amount in breathing and the intercostal muscles to the maximum The feeling of exhaustion is present at all times especially in the morning It is a striking characteristic of most cases Many of the symptoms are precipitated by muscular work, emotion provoking situations and infection

*Signs* —Patients with neurocirculatory asthenia usually manifest tremor of the hands flushing and marked sweating and have a worried expression In addition they usually have a high resting pulse rate an increased respiratory rate and hyperactive knee jerks and ankle jerks These

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auricular node and the left carotid sinus the auriculoventricular node About one out of every five persons has a hypersensitive carotid sinus reflex The sensitivity is increased by age arteriosclerosis a mass in the region of the carotid sinus aortic stenosis and gastrointestinal respiratory and genitourinary disease Parasympathetic drugs like digitalis mecholyl etc also increase it

There are *three types of carotid sinus hypersensitivity* The cardioinhibitory the vasodepressor and the cerebral The first results in cardiac arrest When this type of carotid sinus sensitivity chiefly affects the sinoauricular node ventricular escape may occur when it chiefly affects the auriculoventricular node ventricular standstill with continued auricular beats occurs The second type of carotid sinus hypersensitivity is not very common The cerebral type results in an anoxia of the brain that does not affect cardiac rate or blood pressure the electroencephalogram shows slow high amplitude cerebral waves on the side pressed on There may also be focal neurological signs such as twitching spasm etc on the contralateral side This condition occurs most often upon the development of a sudden decrease in cerebral blood flow in patients with cerebrovascular disease It is a rather rare condition

In the test for carotid sinus sensitivity it is always best to place the patient in the recumbent position and place the stethescope over the heart First the right carotid sinus is pressed upon and then the left Pressure must never be exerted on both sinuses simultaneously The pressure should be removed as soon as the heart is heard to stop beating If these rules are followed the test is harmless Some cases of transient paralysis and thrombosis of the anterior cerebral artery have been reported but this is rather rare In these cases after a period of cardiac arrest or ventricular standstill with the auricle still beating ventricular escape will take place and safeguard the circulation

In the treatment of hyperactive carotid sinus reflexes the first thing to do is to remove the cause This may be a tight collar or disease of the gastrointestinal tract Atropine is very useful to remove overactive vagal tone Sympathomimetic drugs are very helpful Surgery is also occasionally beneficial The carotid sinus nerve has been cut unilaterally or bilaterally for example to eliminate the reflex arc but the results have not been striking The glossopharyngeal nerve has been cut centrally with greater success

The most common cause of syncope is postural vasodepressor type (90 per cent of all cases) The syncope occurs in the upright position and is relieved by recumbency There may be preceding weakness pallor nausea vomiting and sweating The systolic blood pressure falls to between 60 and 80 mm of mercury and the pulse rate drops to 40 or 50 beats a minute This condition results when the blood pressure regulating mechanism fails in the erect position and the flow of blood to the brain is decreased The condition is precipitated by fear anxiety minor injuries bad news venipuncture hemorrhage dehydration and severe infection The treatment consists in returning the patient to the recumbent position and removing the precipitating factor The condition is dangerous in older patients since it may cause death by complicating preexisting heart disease by anoxia

Postural or orthostatic hypotension results from loss of tone in the sympathetic nervous system This is seen after disease of the sympathetic nervous system or after surgery on that system When the patient assumes the upright position the blood pressure falls and syncope results This is the cause of fainting while standing still for long periods of time Treatment consists in using sympathomimetic drugs such as paredrine and ephedrine bandaging the legs and the applying an abdominal support

## THE DISORDERS OF THE HEART BEAT

Normal Cardiac Mechanism —Under normal conditions the impulse which initiates the cardiac contraction originates in the sinus node This highly specialized neuro muscular structure is located in the upper end of the sulcus terminalis at the junction of the superior vena cava and

in poor diastolic filling, decreased minute volume and cerebral anoxia thereby producing syncope. This is most often seen in cases of 1:1 flutter, cases of ventricular tachycardia and ventricular fibrillation. *Myocardial infarction* may result in syncope due either to the sudden fall of blood pressure and shock with decreased blood flow through the brain, or to pain and fear, causing a vasodepressor reflex and resulting in syncope. *Dissecting aneurysms*, particularly of the ascending aorta and transverse arch, may cause syncope by compression of the vessels going to the brain, thus resulting in the decreased cerebral blood flow; syncope may also be due to pain and fear. Furthermore blocks the opening and decreases ventricular filling in certain positions. In cases of *patent interventricular*, or of *patent interauricular septal defect* particularly, there may be at times a reversal of blood flow with the establishment of a right to left shunt; this suddenly decreases the oxygen content of the blood and causes cerebral anoxia and syncope.

But much more common than the primary cardiac causes of syncope is the *syncope* produced by *vagal reflexes*, acting through the *carotid sinus*. These reflexes result either in total cardiac standstill or ventricular standstill with maintenance of auricular rhythm for varying time. These are most

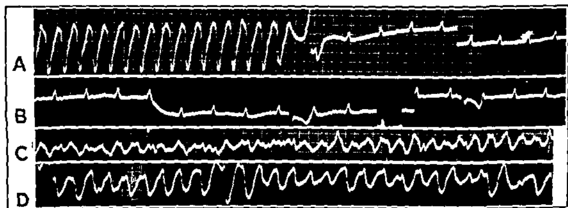



FIG. 140.—*Showing Various Cardiac Mechanisms in Stokes-Adams Attack.*—(A) Initial portion of strip shows a pre-fibrillary type of ventricular tachycardia followed by ventricular standstill. (B) Shows continuation of ventricular standstill with occasional idioventricular beats. (C and D) Show periods of ventricular fibrillation.

*cardiac tamponade* may produce syncope. This will occur when the intrapericardial pressure exceeds the interauricular pressure and decreased cardiac filling results. In *aortic stenosis*, syncope occurs because of the low blood and pulse pressures which inhibits the normal cardiac adjustment to effort or excitement plus associated increased cardio-inhibitory reflexes present in this condition. This may even result in sudden death. Here digitalis should be given very cautiously because it increases the tendency to syncopal attacks. In cases of *mitral stenosis* syncope may occasionally occur in the upright position following excitement. Sometimes the patient has a mural thrombus lodged over the narrow mitral valve; this often seen in older people and may at times actually result in cardiac arrest and death.

The carotid sinus, important in so many reflex cardiac effects, is located at the bifurcation of the carotid artery. The walls of the carotid sinus abound in sensory nerve endings connected by the carotid sinus and the glossopharyngeal nerve with the central nervous system. Afferent fibers come from the eye, the esophagus, the respiratory tract, the gastrointestinal tract, and the genitourinary tract; efferent fibers come from the vagus nerve and the depressor nerve to the aorta and from the vasomotor-center connections. These lead to the sino-auricular or auriculoventricular node. Usually the right carotid sinus chiefly affects the sino-

the ventricular complex the *P-R* interval represents the time required for the impulse to travel from the auricle to the ventricle Normally this interval does not exceed two-tenths second It might be added that the heavy perpendicular lines usually seen on the recording film or paper occur at intervals of two-tenths second The *Q R S* group of the electrocardiogram is produced by the spread of the excitation wave through the ventricles The T wave represents the repolarization stage of the ventricles It is to be noted that the cardiac cycles as depicted by the electrocardiogram follow in an orderly sequence and are identical in every detail indicating that the impulse in each instance arises from the same location and travels the same pathway

the above categories have no irregularity in rhythm It is preferable therefore to use the terms *disorders of the heart beat* and *disturbances of the cardiac mechanism* to describe rhythms in which the pacemaker is not in the sinoauricular node in which there is disturbance in the sinoauricular node in which changes in vagal tone alter the sinus mechanism or in which there is some alteration in conduction after the impulse leaves the sinus node

The causes of these disorders are not entirely understood They may occur in patients with definite myocardial disease of different etiologies during infections as a result of metabolic disturbances anemia and other conditions including toxic states which are discussed below A large number of these disorders are observed however

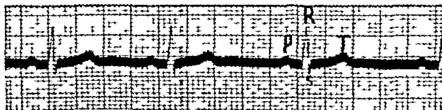



Fig 142 —Normal electrocardiogram Lead II

Cardiac Arrhythmias —Once the normal mechanism of the heart beat is understood it is comparatively easy to classify the disturbances which may occur

A *Disturbances in Vagus and Sinoauricular Node* Sinus arrhythmia sinoauricular heart block sinus bradycardia

B *Disturbances Arising in the Auricle* Auricular extrasystoles auricular paroxysmal tachycardia auricular flutter auricular fibrillation and intra auricular heart block

C *Disturbances Arising in the A V Node* A V heart block (partial complete) A V nodal rhythm nodal extrasystoles nodal tachycardia ventricular or nodal escape

D *Disturbances Arising in the Ventricle* Ventricular extrasystoles ventricular paroxysmal tachycardia ventricular fibrillation pulsus alternans

These are usually classed as cardiac arrhythmias but this term is not a good one as it can be readily seen that many of

in hearts which are clinically normal Some of these are believed to be the result of disturbances in the nervous mechanism indirectly affecting the heart in others the causes are obscure A few such as sinus arrhythmia and other sinus irregularities often occur in hearts which are entirely normal and have no effect in producing myocardial strain directly or indirectly

Clinically it is helpful to know that disorders of the heart beat are rare below the age of 10 years except for sinus arrhythmia In persons from 10 to 20 years of age the types of irregularities encountered are sinus arrhythmia (usually phasic in type) extrasystoles auricular fibrillation and varying degrees of A V heart block

Between the ages of 20 and 30 most of the irregularities observed are those usually seen in rheumatic hearts namely varying degrees of A V heart block auricular fibrillation and extrasystoles From 30 to 40

the right auricle It receives fibers from the vagus and sympathetic nerves which exert a regulating influence on the rate of impulse formation Though any section of the heart is capable of initiating a contraction, the automatic rhythm of the sinus node, under normal circumstances, dominates that of any other section of the heart and therefore governs the cardiac rate and the mechanism of the heart beat The impulses generated at the sinus node spread in a wave-like fashion over the auricles and are conveyed to the ventricle by the auriculo ventricular terminates in an extensive subendocardial network, the Purkinje system, which com municates directly with the muscle fibers The right branch passes down the right side of the interventricular septum and follows the moderator band to the base of the papillary muscles before it begins to break up into its subendocardial ramifications Passing through this highly specialized con duction pathway the impulse which origi nates at the pacemaker activates all of the ventricular musculature The contraction of the auricles is therefore followed in an

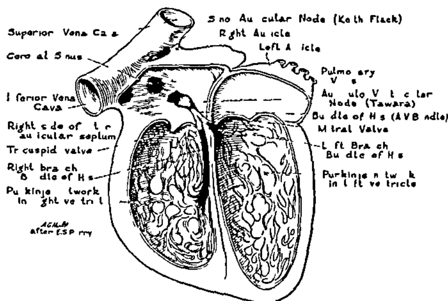



FIG 141—Specialized conduction system of the mammalian heart (diagrammatic) (After F N Wilson in Blumer s Bedside Diagnosis Volume II W B Saunders Company Publishers)

bundle, which represents the only functional connection between the auricle and the ventricle The auriculo-ventricular bundle begins with the auriculo-ventricular node which is located in the base of the auricular septum slightly to the left of the coronary sinus The bundle proceeds forward and to the left to the anterior aspect of the mem branous interventricular septum At this point the bundle divides into two branches the right and the left, going respectively to the right and left ventricles The left branch passes through the membrane im mediately below the junction of the right posterior and the anterior cusps of the aortic valves This branch soon divides and finally orderly fashion by synchronous contraction of the two ventricles

In the electrocardiogram (Fig 142), the the $P$ wave represents the spread of the excitation wave over the auricles The con formation of the wave remains constant for a given individual so long as the excitation wave spreads in the normal fashion It is necessarily altered if the impulse originates outside of the usual location When the impulse arises in the base of the auricles transmission over the auricle is for the most part in the opposite direction to that of the normal and consequently the $P$ wave be comes inverted The interval between the beginning of the $P$ wave and the beginning of

larity Each ventricular contraction is preceded by an auricular systole at the usual intervals Two types of sinus arrhythmia may be observed In the most common the irregularity is phasic varying with the phases of respiration Thus the rate tends to gradually increase with inspiration and decrease with expiration To be a true sinus arrythmia there must be a difference in time between the longest and shortest R R interval of 0 12 seconds Inspiration is an act which tends to diminish vagal tone and expiration tends to increase vagal tone The variations in vagal tone are related to cardiac filling (Bainbridge reflex) and reflexes arising from the pulmonary branches of the vagus The uncommon type of sinus arrhythmia is that in which the irregularity results from digitalis effects and in this instance it is not affected by the phases of respiration

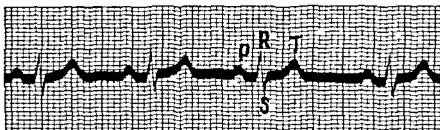



Fig 143 —Sinus arrhythmia Lead II from patient fourteen years of age

Sinus arrhythmia is observed in perfectly normal hearts in children and young adults By itself it is no indication of heart disease However its presence does not exclude heart disease since it is not uncommonly observed in patients with mitral and aortic valvular disease and in the presence of various grades of coronary arteriosclerosis It is said to be absent during active rheumatic fever

*Symptoms* —There are no particular symptoms that are characteristic of sinus arrhythmia

Sinus arrhythmia is usually easily diagnosed The occurrence of a phasic variation in the heart rate as above described is quite characteristic Sometimes the irregularity is so marked that it resembles the more serious types of disorders of the heart action However the restoration of normal rhythm following exercise helps to clarify the diagnosis The electrocardiogram is characteristic No specific treatment is required for sinus arrhythmia

*Other Disorders of Sinus Origin* —Under this heading may be considered sinoauricular heart block and sinus bradycardia In sinoauricular heart block there occurs a sudden decrease in the heart rate, usually almost half the previous normal rate, which may last for one cycle several cycles minutes or hours This condition is observed as a normal finding in individuals who manifest increased vagal tone, in the presence of arteriosclerotic processes involving the sinoauricular node and following digitalis effects It may be produced in a susceptible individual by carotid sinus pressure This condition is so frequently observed in healthy young individuals that it is not considered abnormal when it appears alone Sinoauricular heart block is important under two conditions occasionally the period of block may be prolonged to several seconds resulting in syncopal attacks (*carotid sinus syncope*) Usually however the syncopal attacks are prevented by the temporary assumption of the function of pacemaker by the A V node Sometimes the sinus rate drops to an extremely low figure the A V node failing to receive an impulse initiates the ventricular beating until the sinus node recovers its inherent rhythm This phenomenon is described as a ventricular escape or a nodal escape

The diagnosis of sinoauricular heart block may be suspected clinically but can best be made by means of the electrocardiogram

No treatment is required in those patients presenting no symptoms or signs However

syphilitic heart disease is also encountered While auricular fibrillation is rare, various degrees of A-V heart block extrasystoles and paroxysmal tachycardia are encountered In addition the disturbances in the cardiac mechanism following digitalization are observed *In persons 45 and over one encounters a preponderant number of hearts* of the degenerative type Some of these result from rheumatism hypertension, and syphilis but the majority, especially in the latter decades are the result of coronary arteriosclerosis

The *symptoms* which result from regular heart rates of between 140 and 250 beats a minute vary with many factors In general, the following symptoms are observed palpitation faintness dizziness lightheadedness and at times actual fainting throbbing in the head throbbing in the neck, discomfort in the precordial region shortness of breath and *precordial pain* At times the picture resembles that of shock, and, if the rapid rate persists sufficiently long heart failure may be precipitated even in the presence of a previously normal heart Sudden deaths are not numerous during such rapid heart action

When the heart slows to 20 to 40 beats a minute few symptoms *result* *At times* dyspnea and fatigue on exertion occur because of the lessened output per minute of the heart plus impaired circulatory adjustments At very low pulse rates patients may complain of dizziness and faintness Symptoms of cerebral anoxemia are observed if the heart rate in these patients is lowered still further for brief periods of time Syncopal attacks faintness and even convulsive seizures occur with periods of ventricular standstill ranging from three to nine seconds Irregularities of the heart rhythm may produce little or no subjective symptoms Some patients complain of palpitation thumping of the heart "the heart appears to turn over" Generally the discomfort is moderate but at times the anxiety it produces is considerable and is interpreted as "pain around the heart" thus simulating the anginal syndrome Actually if the irregularity is rapid enough one may get coronary insufficiency and true anginal pain

The ventricular rate often presents a valuable clue relative to the type of disturbance in the cardiac mechanism Ventricular rates below 35 beats per minute when the rhythm is regular suggest complete A V heart block, partial A V heart block or sinus bradycardia *The last two may be* eliminated by emotion, exercise or atropine The ventricular rate in complete A V heart block is usually unaffected by these, since the centers which dominate the ventricular rhythm are not under vagal control Rates between 40 and 50 suggest the presence of A-V nodal rhythm sinus bradycardia, or partial A V heart block A regular rhythm with rates from 140 to 150 suggests the presence of sinus tachycardia auricular paroxysmal tachycardia auricular flutter with 2 to-1 A-V heart block nodal tachycardia or ventricular tachycardia rates ranging from 180 to 220 suggest auricular *paroxysmal tachycardia* *Rates* over 220 suggest the presence of 1 to-1 auricular flutter or a rare type of ventricular tachycardia

In perfectly normal hearts the conditions usually observed are sinus arrhythmia bradycardia sinoauricular heart block, and occasional auricular and ventricular extrasystoles *In rheumatic hearts the usual* disorders observed are varying degrees of partial A-V heart block extrasystoles sinoauricular heart block and auricular fibrillation These effects are of course modified by digitalis In syphilitic hearts the irregularities observed are extrasystoles, A-V heart block and various tachycardias In the degenerative group especially that secondary to coronary artery disease practically any type of irregularity or combination may be observed All these types of heart conditions may be associated with the many disturbances in mechanism resulting from digitalis effects

## Sinus Arrhythmia

Sinus arrhythmia is due to a disturbance in the rhythmic production of impulses at the sinoauricular node and is of vagal origin It is most frequently encountered in children and young adults The auricles and ventricles participate equally in the irregu

larity Each ventricular contraction is preceded by an auricular systole at the usual intervals Two types of sinus arrhythmia may be observed In the most common the irregularity is phasic varying with the phases of respiration Thus the rate tends to gradually increase with inspiration and decrease with expiration To be a true sinus arrythmia there must be a difference in time between the longest and shortest R R interval of 0 12 seconds Inspiration is an act which tends to diminish vagal tone and expiration tends to increase vagal tone The variations in vagal tone are related to cardiac filling (Bainbridge reflex) and reflexes arising from the pulmonary branches of the vagus The uncommon type of sinus arrhythmia is that in which the irregularity results from digitalis effects and in this instance it is not affected by the phases of respiration

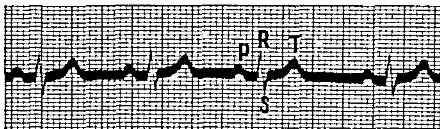


Fig 143 —Sinus arrhythmia Lead II from patient fourteen years of age

Sinus arrhythmia is observed in perfectly normal hearts in children and young adults By itself it is no indication of heart disease However its presence does not exclude heart disease since it is not uncommonly observed in patients with mitral and aortic valvular disease and in the presence of various grades of coronary arteriosclerosis It is said to be absent during active rheumatic fever

*Symptoms* —There are no particular symptoms that are characteristic of sinus arrhythmia

Sinus arrhythmia is usually easily diagnosed The occurrence of a phasic variation in the heart rate as above described is quite characteristic Sometimes the irregularity is so marked that it resembles the more serious types of disorders of the heart action However the restoration of normal rhythm following exercise helps to clarify the diagnosis The electrocardiogram is characteristic No specific treatment is required for sinus arrhythmia

*Other Disorders of Sinus Origin* —Under this heading may be considered sinoauricular heart block and sinus bradycardia In sinoauricular heart block there occurs a sudden decrease in the heart rate usually almost half the previous normal rate which may last for one cycle several cycles minutes or hours This condition is observed as a normal finding in individuals who manifest increased vagal tone in the presence of arteriosclerotic processes involving the sinoauricular node and following digitalis effects It may be produced in a susceptible individual by carotid sinus pressure This condition is so frequently observed in healthy young individuals that it is not considered abnormal when it appears alone Sinoauricular heart block is important under two conditions occasionally the period of block may be prolonged to several seconds resulting in syncopal attacks (carotid sinus syncope) Usually however the syncopal attacks are prevented by the temporary assumption of the function of pacemaker by the A-V node Sometimes the sinus rate drops to an extremely low figure the A-V node, failing to receive an impulse initiates the ventricular beating until the sinus node recovers its inherent rhythm This phenomenon is described as a ventricular escape or a nodal escape

The diagnosis of sinoauricular heart block may be suspected clinically but can best be made by means of the electrocardiogram

No treatment is required in those patients presenting no symptoms or signs However

in the older age group where the sinus rate drops to a low figure with the resultant production of syncopal attacks it is advisable to administer atropine in order to diminish or abolish vagal tone or ephedrine sulfate, 3/8 gr t i d or other sympatheticomimetic drugs. Medication which might increase vagal tone such as digitalis should be omitted.

The prognosis in patients with sinoauricular heart block is good. The rare exception is in those patients who tend to develop syncopal attacks.

## Sinus Bradycardia

Sinus bradycardia is characterized by a slow sinus rate which usually ranges from 30 to 40 beats per minute. Each auricular impulse is followed by a ventricular beat. The low rate is the result of increase in vagal tone. This condition is usually observed in the older age group and is associated with arteriosclerotic changes. These patients usually present relatively few symptoms resulting from the low rate in itself. They are however subject to syncopal attacks if as occasionally happens the rate drops to a still lower figure. These patients present in many respects manifestations which are similar to those described under sinoauricular heart block in the older age group.

## Auricular Flutter

In auricular flutter the cardiac impulse instead of being produced at the normal pacemaker the sinoauricular node is initiated within the muscle surrounding both venae cavae. In this ring of muscle the impulse circulates at a rate the known limits of which are between 220 to 370 per minute. From this starting point these impulses are transmitted to the outlying portion of the auricle. Fortunately the refractory period of the A-V node is much greater than that of the auricular muscle with the result that only a fraction of the auricular impulse passes through the A-V node and is able to produce an effective ventricular beat. In most of the untreated cases a 2 to 1 A-V heart block is present. Rarely the response is 1 to-1 in which case the ventricles which beat at a rate of 240 to 280 per minute rapidly become exhausted. Death may occur in such instances unless the degree of A-V heart block increases spontaneously or vigorous treatment is instituted. Degrees of A-V heart block that range from 3 to 1 and 4 to-1 are occasionally observed occurring spontaneously. More frequently they are observed after digitalis administration.

Recently the circus movement theory concerning the mechanism of auricular flutter, has again been challenged and it is believed that rapid regular impulses spreading in all directions from an ectopic focus produce the flutter waves. The ectopic focus originating the flutter in most instances, is at the caudal end of the auricles and the impulses pass cephalad. The mechanism of auricular flutter, auricular fibrillation premature auricular systole and auricular tachycardia is similar except for the rate of discharge of the ectopic focus. Relatively slow rates of discharge cause premature auricular extrasystoles and paroxysmal tachycardia while the faster rates result in auricular flutter or auricular fibrillation (Prinzmetal).

Attacks of auricular flutter may be established or permanent in which case they last months or years or they may be paroxysmal lasting a few hours or days.

Associated with rapid ventricular rates the ventricular complexes may be widened as in bundle branch block due to fatigue of one of the bundle branches. When the ventricular rate slows down the intraventricular conduction time usually returns to normal.

*Etiology*.—Auricular flutter is usually seen in patients with a moderately advanced or severe grade of myocardial involvement in the middle and older age groups. It is rarely observed in normal hearts. It is more common in males than in females. Auricular flutter is observed most frequently in association with the degenerative group of heart diseases.

*Symptoms and Signs*.—The symptoms and signs of auricular flutter are similar to those of other types of accelerated heart action except for the greater tendency to develop heart failure.

Mental disturbances of varying degrees of severity are observed in about 10 per cent of cases.

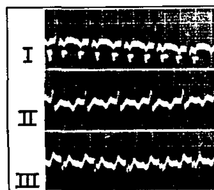
Due to the rapid ventricular rate a pulse deficit is often observed. In many cases there is an associated pulsus alternans. With slow rates in the ventricle (40 to 70 per minute) one may occasionally be able to hear the individual auricular beat. These have been recorded graphically.

Embolic phenomena are observed in approximately 7 per cent of patients with auricular flutter.

*Diagnosis.*—The diagnosis of auricular flutter is to be considered in any patient presenting evidence of an ectopic rhythm with a regular apical rate ranging from 140 to 180 per minute. It must be differentiated from all varieties of paroxysmal tachycardia, from rapid simple tachycardia, and when ventricular response is irregular, from auricular fibrillation. With 3 to 1 and higher grades of A-V heart block it is difficult to diagnose auricular flutter clinically. Carotid sinus pressure in auricular flutter results either in no ventricular slowing or, if this is produced, it is maintained only during the period of carotid sinus pressure, the ventricular rate returning immediately to its original figure when pressure is removed.

The diagnosis of auricular flutter is usually clearly established by the electrocardiogram. Occasionally the tracing fails to clearly show the flutter waves, these being obscured by the QRS complex and T waves. In such instances the auricular waves may be more clearly delineated in the $CR_1$ or $V_1$ or $V_2$ position or may best be shown following carotid sinus pressure, as a result of which auricular cycles are observed unobscured by the ventricular beat.

*Treatment.*—Digitalis is the drug of choice in the treatment of auricular flutter. Digitalis will break up the auricular flutter in about 70 per cent of patients. In most instances the flutter is converted to an auricular fibrillation. Though at times the flutter may be directly converted to a regular sinus rhythm. Once the patient changes from flutter to fibrillation the digitalis is stopped, after which the fibrillation reverts to normal rhythm spontaneously in about two thirds of the patients. If fibrillation tends to persist after a period of one to two weeks quinidine may be tried in an endeavor to convert the auricular fibrillation to a regular rhythm. Occasionally quinidine by increasing the refractory period of auricular muscle



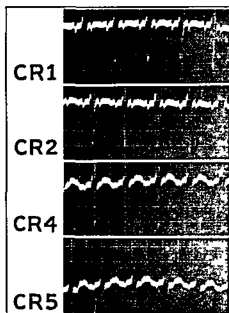




Fig. 144.—Auricular flutter with periods of 2:1 A-V heart block. The P waves are marked in lead I. Note that the precordial leads show distinct auricular deflections in CR1 and CR2 but these are less distinct in CR4 and CR5.

changes fibrillation back to the auricular flutter. Quinidine sulfate is the drug of second choice in the treatment of auricular flutter and for all practical purposes its use should be restricted to those cases where digitalis has failed to break up the flutter. *Quinidine is successful in converting*

in the older age group where the sinus rate drops to a low figure with the resultant production of syncopal attacks it is advisable to administer atropine in order to diminish or abolish vagal tone or ephedrine sulfate 3/8 gr t i d or other sympatheticomimetic drugs Medication which might increase vagal tone such as digitalis, should be omitted

The prognosis in patients with sinoauricular heart block is good The rare exception is in those patients who tend to develop syncopal attacks

## *Sinus Bradycardia*

Sinus bradycardia is characterized by a slow sinus rate which usually ranges from 30 to 40 beats per minute Each auricular impulse is followed by a ventricular beat The low rate is the result of increase in vagal tone This condition is usually observed in the older age group and is associated with arteriosclerotic changes These patients usually present relatively few symptoms resulting from the low rate in itself They are however subject to syncopal attacks if, as occasionally happens the rate drops to a still lower figure These patients present in many respects manifestations which are similar to those described under sinoauricular heart block in the older age group

## Auricular Flutter

In auricular flutter the cardiac impulse instead of being produced at the normal pacemaker the sinoauricular node is initiated within the muscle surrounding both venae cavae In this ring of muscle the impulse circulates at a rate the known limits of which are between 220 to 370 per minute From this starting point these impulses are transmitted to the outlying portion of the auricle Fortunately the refractory period of the A-V node is much greater than that of the auricular muscle with the result that only a fraction of the auricular impulse passes through the A V node and is able to produce an effective ventricular beat In most of the untreated cases a 2-to-1 A-V heart block is present Rarely the response is 1-to-1, in which case the ventricles which beat at a rate of 240 to 280 per minute rapidly become exhausted Death may occur in such instances unless the degree of A-V heart block increases spontaneously or vigorous treatment is instituted Degrees of A V heart block that range from 3 to 1 and 4 to 1 are occasionally observed occurring spontaneously More frequently they are observed after digitalis administration

Recently the circus movement theory concerning the mechanism of auricular flutter, has again been challenged and it is believed that rapid regular impulses spreading in all directions from an ectopic focus produce the flutter waves The ectopic focus originating the flutter, in most instances, is at the caudal end of the auricles and the impulses pass cephalad The mechanism of auricular flutter, auricular fibrillation premature auricular systole and auricular tachycardia is similar except for the rate of discharge of the ectopic focus Relatively slow rates of discharge cause premature auricular extrasystoles and paroxysmal tachycardia while the faster rates result in auricular flutter or auricular fibrillation (Prinzmetal)

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Associated with rapid ventricular rates the ventricular complexes may be widened as in bundle branch block due to fatigue of one of the bundle branches When the ventricular rate slows down the intraventricular conduction time usually returns to normal

*Etiology* — Auricular flutter is usually seen in patients with a moderately advanced or severe grade of myocardial involvement in the middle and older age groups It is rarely observed in normal hearts It is more common in males than in females Auricular flutter is observed most frequently in association with the degenerative group of heart diseases

*Symptoms and Signs* — The symptoms and signs of auricular flutter are similar to those of other types of accelerated heart action except for the greater tendency to develop heart failure

*Etiology*.—Auricular fibrillation is almost always observed in the presence of myocardial disease frequently of an advanced grade. It is rarely observed in normal hearts. The arrhythmia is observed in 60 per cent of the patients with heart failure. The most frequent associated factor is hypertensive arteriosclerotic cardiovascular disease, the next most frequent is rheumatic heart disease. These two conditions account for about 90 per cent of the cases of auricular fibrillation. Other associated factors are thyrotoxicosis and toxic states. It is also frequently seen in interauricular septal defects. It is rarely observed in syphilitic heart disease. *Auricular fibrillation is rare* below the age of 15; it is more common in men than in women, but the preponderance of males is chiefly in the non-rheumatic group, while in the rheumatic group the incidence is about equal.

*Symptoms and Signs*.—Patients with auricular fibrillation almost invariably demonstrate evidence of myocardial abnormality, often of a severe grade. They usually manifest evidence of heart dysfunction, namely, breathlessness, fatigue on slight exertion, precordial oppression, cyanosis, cardiac enlargement, rales at the lung bases, pleural effusion, edema of the legs and ascites, though there are those who go on for many years with no symptoms at all.

Auscultation reveals a characteristic type of irregular irregularity. This is most pronounced clinically at rates ranging from 90 to 130 per minute. When the ventricular rate is slow or very rapid the typical irregularity is difficult to determine clinically.

At fairly rapid rates during a short cardiac cycle the ventricular contraction often fails to lift the aortic valve. As a result only one heart sound is heard and the ventricular contraction is too weak to produce a pulse at the wrist. When many of these contractions occur it leads to a marked variation between the apical and pulse rates and this difference is known as a pulse deficit.

The heart sounds vary considerably in intensity, the louder sounds are heard following the longer pauses which permit greater ventricular filling. Cardiac murmurs undergo significant changes with the onset of auricular fibrillation. Systolic murmurs vary considerably in intensity depending on the length of the preceding cycle and consequent variation in ventricular filling; they are louder following the longer cycles and fainter after the shorter cycles. With rapid rates the murmurs become inaudible. The presystolic murmur of mitral stenosis, due to failure of the auricles to contract, is re-

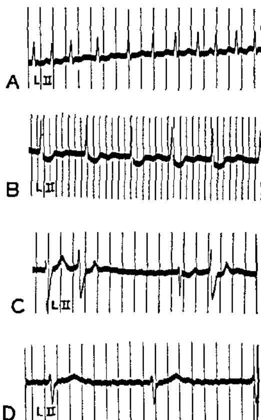



FIG 145.—*Auricular Fibrillation Showing Varying Degrees of A-V Heart Block.* (A) Auricular fibrillation with rapid ventricular rate which averages 160 per minute. (B) After digitalization the ventricular rate is dropped to about 70 per minute. The ST segments are depressed. (C) Early toxic effects as indicated by low ventricular rate with coupled extrasystoles (ventricular or nodal). (D) Auricular fibrillation with almost complete A-V heart block. Ventricular rate is about 32 per minute.

placed by a diastolic rumble with the onset of auricular fibrillation. Its intensity and the phase of diastole when it is heard vary with the cycle length.

*Pathology*.—The pathology of auricular fibrillation is that of the associated disease as mentioned above. In long-standing cases

auricular flutter to a normal sinus rhythm in 20 to 30 per cent of the cases This drug is a protoplasmic poison and should be used with caution especially where large doses are required and in the presence of severe myocardial damage In the presence of congestive heart failure *it should be used only* rarely Quinidine when successful converts the flutter directly to regular sinus rhythm without an intermediate period of auricular fibrillation Before normal rhythm is restored quinidine slows the rate of auricular beating by its direct muscular effect on the auricle In flutter, the auricular rate under quinidine may drop as low as 135 per minute As a result of paralysis of the vagal fibers supplying the A-V node, the degree of the A-V heart block may change from 2-to-1 to 1-to-1 so that with an auricular rate of 135 per minute, the ventricular response may also be 135 per minute Under these conditions the likelihood of heart failure in an exhausted heart muscle is very great hence this period of rapid ventricular rate must be as short as possible

Observation of the effects of digitalis and quinidine on the fibrillating auricle shows that both agents depress auricular conductivity at rapid auricular rates and thereby lower the fibrillating threshold (Prinzmetal)

Acetyl beta methylcholine has also been used in auricular flutter, but the profound drop in blood pressure and the severe side effects of nausea vomiting sweating and abdominal cramps produced by this drug make its use undesirable in the treatment of flutter

In those cases where auricular flutter is associated with a rapid ventricular rate and heart failure since absorption of the drug may be slow or uncertain one may resort to the use of an intravenous or intramuscular preparation The latter is somewhat safer For intravenous use one may give strophanthin 0 6 mgm digitoxin (1 2 mgm) digoxin (1 5 mgm) or cedilanid (1 6 mgm) Digalin in 3 to 5 cat unit doses may be used intramuscularly Additional doses may be given in from 2 to 4 hours, as needed

*Prognosis* —The prognosis depends on the duration of the flutter the ventricular rate the condition of the myocardium and the response to treatment Instances of auricular flutter have been known to last uninterruptedly for from five to ten years This duration, however, is unusual As a rule, auricular flutter occurring in older individuals is associated with a relatively poor prognosis

### AURICULAR FIBRILLATION

In auricular fibrillation the impulse instead of being initiated in the normal pacemaker the sinoauricular node, starts in a ring of muscle surrounding the superior vena cava, the inferior vena cava or both venae cavae The impulse continues to circulate in one of these rings of muscle in a manner similar to that of auricular flutter with the difference that the rate is much higher, ranging from 450 to 700 per minute averaging a rate of 550 per minute These waves are propagated to the auricular muscle but instead of traveling in a regular pathway as in auricular flutter encounter islands of refractory tissue so that their pathway varies from beat to beat This results in a variation in the cycle length and in the shape of the auricular complexes In auricular fibrillation there is no concerted contraction of the auricles as in flutter the auricles are in a continuous state of diastole and the auricular muscle is pervaded by numerous fibrillary twitchings This so called circus movement theory of Sir Thomas Lewis was challenged many years ago by German workers and has recently been challenged again by workers in this country The final answer is yet to be given

In the average untreated case of auricular fibrillation the ventricular rate ranges from 110 to 150 per minute Occasionally the rate may rise to 160 to 200 per minute Such high rates in older patients with arteriosclerotic heart disease may precipitate an attack of heart failure frequently accompanied by the picture of shock At times one may encounter auricular fibrillation where the ventricular rate without digitalis therapy ranges from 40 to 60 per minute Such instances are usually observed in older patients who have coronary arteriosclerosis and sclerotic changes in the A V node

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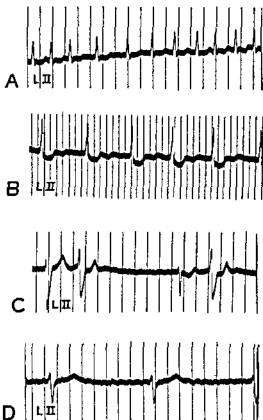



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placed by a diastolic rumble with the onset of auricular fibrillation. Its intensity and the phase of diastole when it is heard vary with the cycle length.

*Pathology*.—The pathology of auricular fibrillation is that of the associated disease as mentioned above. In long standing cases

particularly those of rheumatic etiology, mural thrombi form in the auricular appendages and in the pectinate muscles. These are dislodged frequently, resulting in emboli to the brain, lungs, abdominal viscera and the lower extremities.

*Diagnosis*.—The diagnosis of auricular fibrillation may be suspected clinically in a patient manifesting an irregular type of irregularity. The characteristic symptoms and signs have been discussed above. Clinically, auricular fibrillation must be differentiated from multiple extrasystoles arising from different foci and auricular flutter associated with varying degrees of heart block. In the first two conditions exercise tends to make the rhythm quite regular, whereas in auricular fibrillation the rhythm becomes more irregular. The electrocardiogram usually establishes the diagnosis without doubt.

*Treatment*.—Since auricular fibrillation is usually associated with varying degrees of heart failure, therapy should be directed to this state in addition to the treatment of the irregularity. Digitalis is the drug of choice in the treatment of auricular fibrillation. It is in this condition that the greatest hopes for digitalis have been realized. Digitalis acts by impeding the passage of impulses from auricle to ventricle and thus slowing the rate. This is accomplished in two ways: by direct muscular effect and by a vagal effect on the A-V node. The maximum therapeutic effect is said to be reached when the apical rate drops to about 70 per minute with an elimination of the pulsus deficit. Digitalization may be performed rapidly in patients with a severe grade of heart failure and rapid rates or slowly in those where failure is slight or moderate in degree.

The approximate dose required for a 150 pound person is about 1.3 Gm. of the powdered leaf. This dose may be given over a period of 4 to 5 days when slow digitalization is adequate or within 1 to 2 days when rapid digitalization is necessary. When the patient presents a picture of severe congestive failure necessitating rapid digitalization and positive absorption, the parenteral route is indicated. Strophanthin 0.6 mgm. may be given intravenously, followed in 2 to 3 hours by 0.3 mgm. This last dose may be repeated if necessary in about 6 hours. Digalen, 2 to 3 cat units, may be administered intramuscularly and repeated 1 or 2 times in 6 to 8 hours, depending on the effect of previous doses on the heart. The digitalis glycosides may also be used in the doses as given for the treatment of heart failure. However, no matter what digitalis product is used, the patient's reaction will be the guide to dosage. Digitalis is contraindicated in patients with a slow ventricular rate, that is, below 50 per minute (independent of treatment) and this drug should not be given where the ventricular rate following therapy has decreased to 40 or 50 beats per minute. In such cases further slowing of the ventricular rate does harm by increasing the diastolic volume, which leads to stretching of the already diseased cardiac fibers. The dosage of digitalis necessary to produce this therapeutic effect varies considerably depending on the age of the patient and the underlying pathologic state, particularly the sclerotic changes in the A-V node in the older age group. Mercurial diuretics may also be used to overcome cardiac failure if this is present.

In the presence of thyrotoxicosis, toxic states and increased sympathetic tone, the dosage required to maintain a ventricular rate of from 70 to 80 per minute is usually higher than the average dose. On the other hand in older patients with sclerotic changes in the A-V node and those with overactive vagal tone, smaller doses usually suffice to slow the ventricular rate. Patients with aortic stenosis particularly are often sensitive to digitalis and usually can tolerate small doses only. It should be emphasized that an apical rate of 60 to 70 does not necessarily coincide with the maximum degree of improvement as far as congestive signs are concerned. Frequently edema may be present even at these slow rates. In such instances digitalis should not be further pushed. Instead the congestive signs should be treated by diuretics and other procedures such as low sodium diets.

Toxic effects of digitalis manifest themselves by the appearance of numerous ventricular extrasystoles, coupled rhythm, and sequences of two or more ventricular beat

With continuance of the drug ventricular paroxysmal tachycardia results. This is a dangerous type of arrhythmia since it predisposes the patient to ventricular fibrillation which is practically incompatible with life. It should be emphasized that these toxic effects may occur in the absence of nausea, vomiting, and other frequently mentioned toxic manifestations. These ectopic rhythms may be avoided by careful supervision of the digitalis dosage and by carefully following the patients both clinically and electrocardiographically. When such toxic effects appear, digitalis should be stopped immediately. Should they continue to the stage of ventricular tachycardia, quinidine sulfate may be administered in an endeavor to abolish this arrhythmia. Recently procaine amide (250 mg. to 1 gm. every 4 hours) has been found to be equally, if not more effective than quinidine for the treatment of ventricular tachycardia.

The continuance of auricular fibrillation involves three problems: the circulatory dynamics are relatively inefficient as compared to what is present with normal rhythm, continuous digitalization is necessary, and most important there is a constant danger of embolic phenomena leading to serious complications depending on the organ involved.

Quinidine sulfate may be administered to patients with auricular fibrillation where it is desired to convert the irregularity to a normal sinus rhythm. It is indicated where the onset of fibrillation is relatively recent, where the heart is not severely diseased and where the auricles, as observed fluoroscopically, are not greatly enlarged. In such cases quinidine is efficient in converting the fibrillation to normal rhythm in over 50 per cent of patients. Frequently quinidine administration must be maintained for two to three months after normal rhythm has been restored since cessation may lead to the return of auricular fibrillation. Quinidine sulfate is also indicated in the prevention of attacks of paroxysmal auricular fibrillation. The dose of quinidine varies from 0.366 Gm. to 0.6 Gm. every 2 hours for 10 doses unless the attack of fibrillation is terminated earlier.

One of the dangers to be considered in the restoration of normal rhythm is the possibility of emboli being thrown off into the circulation. Statistics relative to this occurrence vary considerably because it is difficult to differentiate embolic phenomena which occur as a result of the restoration of normal rhythm from those which occur as a result of the underlying cardiac state. In those cases where the fibrillation is of less than three months' duration the danger of embolic phenomena is slight as compared to the benefits to be derived. This danger of embolization can now be markedly reduced by anticoagulant therapy. The patient is given enough anticoagulant to bring the prothrombin time to about three times normal, then the quinidine is given while anticoagulant therapy is maintained. This has apparently reduced the danger of embolization.

Auricular fibrillation which results from thyrotoxicosis usually disappears following successful thyroid surgery with restoration of basal metabolism to normal. Quinidine may be of help to those patients in whom the restoration of normal rhythm is somewhat delayed.

Auricular fibrillation which results from rheumatic activity, some toxic process or disturbance of metabolism tends to return to normal rhythm with the cessation of these processes unless the damage to the auricular muscle has been severe with resultant irreversible changes.

*Prognosis.*—The prognosis in auricular fibrillation depends on the age of the patient, the underlying cardiac condition, the presence of cardiac enlargement, the presence of heart failure, and the ease with which the apical rate and heart failure are controlled. In addition complicating factors such as renal or cerebral disease or the presence of embolic phenomena may modify the prognosis.

## Paroxysmal Auricular Tachycardia

In paroxysmal auricular tachycardia the cardiac impulse, instead of originating in the normal pacemaker, the sinoauricular node, starts from a focus situated anywhere in the auricles outside the normal site of origin. The paroxysms usually start suddenly, last a few seconds, hours or days, and usually

end suddenly The known limits of the auricular rate range from 140 to 220 per minute Patients subject to these paroxysms often present a history of isolated auricular extrasystoles which gradually become more numerous, occur more frequently, and later appear as a sequence of two or more beats If six auricular extrasystoles are observed occurring in succession they may be said to constitute a short paroxysm of auricular tachycardia Because of their ectopic origin, the P waves during the paroxysm vary in configuration to a greater or lesser degree from those observed during the normal mechanism As in auricular extrasystoles they may be flattened, upright or inverted With rapid rates, the P waves blend with or may be submerged in the T waves The P-R intervals are slightly but not significantly shortened by the tachycardia

The QRS complexes in auricular tachycardia usually possess the normal configuration Associated with rapid ventricular rates, however the ventricular complexes may be widened, probably the result of fatigue of one of the bundle branches

Two types of auricular paroxysmal tachycardia may be observed In the common type the ventricles respond to every beat of the auricles, in the less common type the auricular tachycardia is associated with varying degrees of A-V heart block so that with an auricular rate which ranges from 150 to 200 per minute the ventricular rate is 75 or 100 per minute

Patients subject to attacks of paroxysmal auricular tachycardia sometimes present electrocardiograms which during the period of normal rhythm show a short P R interval with a widened QRS complex (Wolff-Parkinson-White syndrome ) Aside from the tendency of these patients to develop this arrhythmia their hearts are usually normal clinically

*Etiology* —The underlying etiology in paroxysmal auricular tachycardia is not known Since this disturbance is observed in a considerable number of hearts (about 50 per cent) which are considered to be clinically normal various theories for its production have been advanced Among them are disturbances of the physiochemical mechanism in the auricles, allergic states and high degrees of sympathetic tone In the remaining 50 per cent this condition is observed in the presence of damage to the auricular muscle in patients with rheumatic, hypertensive and arteriosclerotic heart disease, and in toxic states The type of auricular tachycardia associated with A-V heart block is observed usually in the older age groups in association (1) with toxic digitalis effects and (2) in the presence of coronary arteriosclerosis

*Symptoms and Signs* —The symptoms of auricular paroxysmal tachycardia are similar to those observed in the presence of any ectopic rhythm and depend largely on the state of the heart muscle and its response to an acceleration of the heart beat, the duration of the paroxysm and the nervous make-up of the patient These may vary from a relative freedom from symptoms except for slight palpitation to varying degrees of precordial discomfort and a feeling of marked anxiety associated with considerable precordial pain

The signs of auricular paroxysmal tachycardia are those of an accelerated heart action superimposed on the types of hearts mentioned above Gallop rhythm and pulsus alternans are encountered not infrequently during the paroxysm Heart failure and the anginal syndrome may also be observed Occasionally especially in the older age group with arteriosclerosis, the paroxysm may precipitate the picture of shock resembling that of an acute myocardial infarction While deaths occurring during paroxysmal auricular tachycardia are rare they have been observed

*Pathology* —The pathology of auricular paroxysmal tachycardia is that of the underlying states mentioned above No specific pathology has been described

*Diagnosis* —The diagnosis of auricular paroxysmal tachycardia should be suspected in a patient who gives a history of a sudden acceleration of the heart beat which lasts for varying periods of time and stops suddenly The presence in the past of auricular extrasystoles is suggestive evidence The presence of a regular rhythm during the paroxysm the rate of which ranges from 140 to 220 per minute should lead one to suspect

auricular paroxysmal tachycardia as the cause. The differential diagnosis involves simple tachycardia, auricular flutter, and ventricular tachycardia. Of these three abnormal mechanisms, paroxysmal auricular tachycardia is the only one which, when responding to carotid sinus pressure, results in a sudden restoration of the normal mechanism, the latter being maintained for relatively long periods of time. Ventricular tachycardia is uninfluenced by carotid sinus pressure and in auricular flutter a slowing of ventricular rate, if obtained, is maintained only during the period of carotid sinus stimulation. Some patients with a sinus tachycardia and a sensitive carotid sinus mechanism may also develop a slowing of the rate during pressure with a rapid return to the original rate on relief of the pressure. The final diagnosis is usually clearly established by the electrocardiogram.

*Treatment.*—The treatment of simple paroxysmal tachycardia may be divided into (a) treatment during attacks and (b) treatment between attacks.

(a) During the attack, the following procedures may be tried: application of carotid sinus pressure. In order to properly apply this pressure the patient should be placed in the recumbent or semi-recumbent position. The carotid artery should be palpated as high up in the neck as possible and pressed firmly against the vertebral column. This vessel is frequently an elusive structure and one must make certain that the carotid artery and not soft tissue of the neck is pressed upon as described above. During the maintenence of pressure a stethoscope should be continually applied to the precordium and as soon as the heart stops the pressing finger should be immediately removed. Simultaneous bilateral carotid sinus pressure should never be applied. We have never seen any accidents result from this procedure when applied as directed above though permanent and transient hemiplegias have been reported in a few cases. Ocular pressure is not advised routinely because of untoward effects which have been observed. The patient himself as a result of experience frequently employs similar procedures such as pressure applied to various parts of the neck, particularly in the region of the carotid sinus, bending down, stretching the neck as far back as possible, holding the breath, yawning, or inserting the hand in the throat to induce vomiting. These procedures have vagal stimulation as their basis.

The following drugs may be given during the paroxysm if carotid sinus pressure fails to restore normal rhythm.

(1) Digitalis intramuscularly, 2 to 3 cat units repeated in one to two hours if necessary. The intravenous route has also been recommended but we rarely find this necessary. Carotid sinus pressure, if previously ineffective, frequently slows the heart beat after digitalis administration.

(2) Magnesium sulfate—10 cc. of a 20% solution administered intravenously.

(3) Calcium gluconate—10 cc. of a 10% solution intravenously. If efficacious the paroxysm will stop immediately.

(4) Quinidine sulfate—0.3 Gm. intramuscularly hourly for 5 to 6 doses or for longer periods. Quinine dihydrochloride—0.3 Gm. diluted in 20 to 50 cc. of normal saline may be given slowly intravenously or the same dose diluted to 5 or 10 cc. may be given subcutaneously. Quinidine may be given by mouth in a dose of 0.2 to 0.3 Gm. every hour for ten or more doses.

(5) Mecholyl—25 to 50 mg. subcutaneously. This often results in cessation of the paroxysm, however this drug usually produces a profound fall in the systemic blood pressure. Periods of ventricular fibrillation after its administration have been observed. It should be used cautiously in the very young, the very old, and in asthmatic individuals. When the drug is given one should always have a syringe of 1.2 mgm. of atropine ready to counteract untoward effects.

(6) Ipecac—may be given by mouth in the form of the syrup in a dose of 4 to 15 cc. to induce vomiting.

(7) Prostigmine—1 to 2 cc. of 1:2000 solution is given intramuscularly. While it may not be effective in itself it increases the sensitivity of the carotid sinus about 20 minutes after its administration so that it frequently renders the previously insensitive carotid sinus sensitive to carotid sinus stimulation.

(8) Fugarin—though toxic in some cases may stop attacks.

(9) Neosynephrine—given intravenously in 0.5 to 2.0 mgm. doses may restore normal rhythm in less than a minute. This action is attributable to reflex cardiac inhibition elicited by the rapid rise in pressure in the carotid sinuses and aortic arch.

(10) Other sympatheolytic drugs such as tetraethyl ammonium chloride are effective in stopping paroxysms, but their use is not desirable because of their generalized effect.

(11) Pronestyl (procaine amide) in doses of 250 mgm. to 1 Gm. every 4 hours has recently been found to be effective in some cases.

(b) The treatment between attacks involves ascertaining the precipitating cause of the attacks if possible and treating it. Nervous states, abdominal distension, excessive exertion and allergic factors may all be provocative causes. If the paroxysms occur frequently, the following procedures are usually helpful: quinidine sulfate—0.2 Gm, four to five times per day; digitalization followed by a maintenance dose which may be continued for months. Prostigmine bromide 15 mgm. 4 times daily orally has also been advised. Occasional cases are encountered where these procedures do not suffice and paroxysms continue. Then thoracic sympathectomy has been suggested as a remedy. This procedure by reducing sympathetic cardiac effects has been successful in stopping paroxysms in a certain number of cases.

*Prognosis.*—The prognosis of paroxysmal auricular tachycardia is usually good in so far as individual attacks are concerned except (a) in a long continued paroxysm, (b) when severe myocardial damage is present, (c) and in those infrequent instances where the attacks recur repeatedly in spite of therapy.

## Auriculoventricular Heart Block

A-V heart block may be divided into two types, partial and complete. The first stage of A-V heart block is said to occur when the A-V conduction time (P-R interval) exceeds 0.20 second. As the degree of block increases the A-V conduction time becomes longer and longer until dropped beats occur, that is, the ventricles fail to respond to some auricular beats. This particular type of partial block is known as the Wenckebach phenomenon. In a still higher grade of block there may be observed 2 to 1, 3 to 1, 4 to 1 or a still higher degree of partial A-V heart block. As the block further increases a stage is reached when the ventricles fail to respond to any auricular impulses, with the result that these two chambers beat entirely independent of each other. When this stage is reached *the degree of A-V heart block is said to be complete.*

In complete A-V heart block the auricles beat regularly at a rate of 70 to 80 per minute in response to their pacemaker, the sinoauricular node, and the ventricles also beat regularly at a rate of 20 to 40 per minute in response to their center located either in the lower portion of the A-V node or the upper portion of the interventricular septum. In complete A-V heart block the auricles and ventricles beat entirely independently of each other. The auricular rate is influenced by the vagus and its rate can be speeded by emotion, exercise or atropine. These factors do not affect the ventricular rate since it is no longer controlled by the vagus. The ventricular rate in complete heart block may rarely be affected by marked changes in the sympathetic tone such as that produced following the injection of adrenalin or in fever. The ventricular rate in complete A-V heart block rarely exceeds 40 per minute. Under certain conditions the ventricular rate may reach 70 to 100 per minute; this may occur following toxic digitalis effects and in anoxic states, for example, immediately after emergence from a Stokes-Adams seizure.

*Etiology.*—A-V heart block may occur at any age. Partial A-V heart block in individuals below the age of 35 is due usually either to digitalis effects or to rheumatic involvement in the acute, subacute or healed stage. In acute rheumatic fever prolongation of the A-V conduction time is usually observed as an extremely transient phenomenon. However, it is occasionally observed in a healed stage many years after the acute rheumatic infection has subsided.

Minor grades of A-V heart block may be observed in many conditions, for example

congenital heart disease rheumatoid arthritis subacute bacterial endocarditis and other infections Recently doubt has been cast upon the specificity of a prolongation of the P R interval in the diagnosis of rheumatic fever in the younger age group This is due to the increasing frequency with which prolongation of the A V conduction time has been observed in other infections for example mumps poliomyelitis etc Rarely is it observed in syphilis and occasionally it is seen in the absence of demonstrable heart disease The position of the patient has recently been shown to affect the P R interval In some subjects prolongation has been noted in the recumbent position when it was absent with the patient sitting upright

*Pathology* —In partial A-V heart block the pathology depends on the underlying disease If the result of rheumatic fever one may observe Aschoff bodies in various stages of healing cellular infiltration and isolated areas of fibrosis Other infections also produce inflammatory and toxic changes which may impair conduction through this tissue In sclerotic processes the A V node is partially or almost entirely replaced by fibrous tissue with only islands of muscle tissue remaining Occasionally the A-V node is severed by a calcareous plaque In another type of complete A V block the lesion is observed as a fibrotic scar severing both bundle branches as they emerge from the bundle of His Gummata occurring in the A V node or the bundle of His are rare

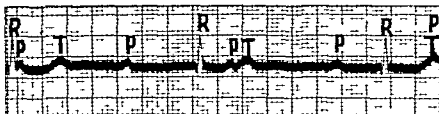



Fig 146 —Complete auriculo-ventricular block Lead I

Above the age of 35 rheumatic heart disease is a less important factor digitalis and other conditions are to be considered as causative In the later decades coronary artery disease and sclerotic processes involving the A-V node are chiefly responsible Syphilis is rarely a factor In complete A V heart block the preponderating causes are coronary arteriosclerosis and sclerotic processes involving the A V node Rare causes are congenital heart disease gumma and acute coronary occlusion involving the right coronary artery at the point where it turns sharply to become the posterior descending branch of the right coronary artery

Recently attention has been focused on a group of patients who develop A V heart block of varying grades due to vagal stimulation caused by reflexes originating in the gastrointestinal tract and other portions of the body and following local constriction about the neck in the region of the carotid sinus

In some cases no organic pathologic cause for the block can be found

*Symptoms and Signs* —In partial A V heart block no symptoms may be observed due to the block itself even with a slow ventricular rate The symptoms are those of the underlying disease Some cases of complete A V heart block present no symptoms Others complain of fatigue on exertion consciousness of the heart slowly beating and occasional precordial pain These patients usually cannot engage in strenuous physical exertion but usually do fairly well on a reduced physical regimen

As a result of the slow rate alterations in the cardiovascular dynamics appear The cardiac output per beat is increased but the cardiac output per minute is decreased The systolic blood pressure rises to about 170 to 200 per minute and left ventricular hypertrophy results These patients are subject to Stokes Adams attacks which are discussed below

(9) Neosynephrine—given intravenously in 0.5 to 2.5 mgm. doses, may restore normal rhythm in less than a minute. This action is attributable to reflex cardiac inhibition elicited by the rapid rise in pressure in the carotid sinuses and aortic arch.

(10) Other sympatheolytic drugs such as tetraethyl ammonium chloride are effective in stopping paroxysms, but their use is not desirable because of their generalized effect.

(11) Pronestyl (procaine amide) in doses of 250 mgm. to 1 Gm. every 4 hours has recently been found to be effective in some cases.

(b) The treatment between attacks involves ascertaining the precipitating cause of the attacks if possible and treating it. Nervous states, abdominal distension, excessive exertion and allergic factors may all be provocative causes. If the paroxysms occur frequently, the following procedures are usually helpful: quinidine sulfate—0.2 Gm. four to five times per day; digitalization followed by a maintenance dose which may be continued for months. Prostigmine bromide 15 mgm. 4 times daily orally has also been advised. Occasional cases are encountered where these procedures do not suffice and paroxysms continue. Then thoracic sympathectomy has been suggested as a remedy. This procedure by reducing sympathetic cardiac effects has been successful in stopping paroxysms in a certain number of cases.

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In complete A-V heart block the auricles beat regularly at a rate of 70 to 80 per minute in response to their pacemaker, the sinoauricular node, and the ventricles also beat regularly at a rate of 20 to 40 per minute in response to their center located either in the lower portion of the A-V node or the upper portion of the interventricular septum. In complete A-V heart block the auricles and ventricles beat entirely independently of each other. The auricular rate is influenced by the vagus and its rate can be speeded by emotion, exercise or atropine. These factors do not affect the ventricular rate since it is no longer controlled by the vagus. The ventricular rate in complete heart block may rarely be affected by marked changes in the sympathetic tone such as that produced following the injection of adrenalin or in fever. The ventricular rate in complete A-V heart block rarely exceeds 40 per minute. Under certain conditions the ventricular rate may reach 70 to 100 per minute; this may occur following toxic digitalis effects and in anoxic states, for example, immediately after emergence from a Stokes-Adams seizure.

*Etiology.*—A-V heart block may occur at any age. Partial A-V heart block in individuals below the age of 35 is due usually either to digitalis effects or to rheumatic involvement in the acute, subacute or healed stage. In acute rheumatic fever prolongation of the A-V conduction time is usually observed as an extremely transient phenomenon. However, it is occasionally observed in a healed stage many years after the acute rheumatic infection has subsided.

Minor grades of A-V heart block may be observed in many conditions, for example

Procaine amide may be tried when the above drugs fail

*Prognosis* —The prognosis of partial A-V heart block depends on the underlying etiology and can best be determined by evaluation of the heart as a whole The heart block in itself does not kill Most of these patients die from heart failure or the underlying disease Occasionally cases are observed which change from partial to complete A V heart block and back again

Complete A V heart block is much more serious although instances where such patients have lived 10 to 20 years have been recorded The patient except in rare instances *must live a sedentary existence* especially if subject to Stokes-Adams attacks No therapy for the block itself is required if the patient is free of seizures

muscle In some instances this is clearly the result of disease of the heart muscle resulting from various etiologies inflammatory degenerative or toxic states anoxia and poisons especially digitalis In many instances the exact cause is not revealed even after careful clinical examination and investigation Two theories have been advanced for the production of extrasystoles (1) that of re-entry suggests that the normal beat stimulates a portion of the heart muscle to produce the ectopic beat (2) that of parasystole which suggests that in addition to the normal pacemaker another center is active in the heart muscle producing extrasystolic beats independently at all times but breaking through the regular rhythm only occasionally

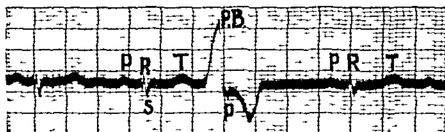



Fig 147 —Ventricular premature beat with retrograde stimulation of the auricles Lead III

## Extrasystoles or Premature Contractions

The normal rhythm consists of a regular sequence of beats arising in the sinoauricular node transmitted to the auricles and then through the A V node to the ventricles Each impulse is part of a rhythmic series The extrasystoles arise prematurely thus disturbing the rhythmic series of beats and may be followed by a compensatory pause Extrasystoles may arise in the auricles, the ventricles or the A V nodal tissue Premature contractions arising in the ventricles *are always followed* by a compensatory pause (except in the rare type of interpolated extrasystoles) in auricular and nodal premature beats the following cycle is usually less than that of a compensatory pause The exact cause or mode of production of extrasystoles *is not known* They apparently arise from an irritable focus in the heart

*Etiology* —The etiology underlying extrasystoles is not well known Often they occur in hearts that are clinically normal Premature beats have been recorded at all ages They are rare in the first decade their incidence is greatest in the age groups between 50 and 70 years Such beats may be observed singly or in groups of two or three The following conditions are known to produce extrasystoles infectious diseases especially rheumatic fever scarlet fever and diphtheria toxic digitalis effects severe grades of myocardial disease for example coronary occlusion and anoxic states foci of infection overactivity of the sympathetic system may exaggerate the tendency to produce extrasystoles especially if they are already present certain psychoneurotic states reflexes from gastrointestinal disturbances tobacco and coffee are probably overrated as causes posture is often a factor usually they are more frequent in the re

*Diagnosis*.—With prolongation of the conduction time (prolonged P-R interval) there results a diminished intensity of the first heart sound which may be marked. If the P-R interval is sufficiently prolonged it may produce a gallop sound (summation gallop). This gallop sound is heard best at rates over 100 per minute and is the result of auricular contraction superimposed upon the wave of early diastolic ventricular filling. With a higher grade of partial block, dropped beats may be detected. These pauses may be abolished by exercise; they are at times difficult to differentiate from the compensatory pause following an extrasystole. Occasionally the auricular sounds may be audible in the higher grades of A-V heart block.

When the heart beats regularly between 30 to 50 per minute, an A-V heart block may be suspected. In partial block exercise or amyl nitrite abruptly doubles the ventricular rate. When the apical rate is regular and ranges from 20 to 40 per minute and is unaffected by exercise or atropine, complete A-V heart block should be suspected. The first heart sound varies in intensity because of the varying A-V intervals. When the auricular and ventricular contractions occur close together the first sound is relatively loud; when they are far apart the first sound is faint.

The important symptoms to be considered in the higher grades of partial and complete block are the development of giddiness, fainting, and temporary loss of consciousness (Stokes-Adams syndrome). These seizures occur during the transition from partial to complete heart block as well as during the course of complete A-V heart block. They result from periods of asystole which last from 3 to 9 seconds or longer and consist of syncopal attacks or actual convulsive seizures. The following are the underlying mechanisms recorded electrocardiographically during the seizures: (a) a prefibrillary type of ventricular tachycardia, (b) ventricular fibrillation, (c) standstill of the whole heart, (d) ventricular standstill with maintenance of auricular beating. These mechanisms may occur either singly or in combination. Recognition of these various types is important in therapy. Death frequently occurs during a Stokes Adams seizure; indeed, this is the most frequent cause of death in complete A-V heart block. The patient may experience many seizures before death finally supervenes, sometimes over a period of 3 to 5 years.

*Treatment*.—No treatment is required for minor grades of A-V heart block. The treatment is that of the underlying cause if ascertained, for example, rheumatic heart disease or other infection. Although digitalis may be given to patients with A-V heart block, one should be somewhat more cautious on its administration because of the greater susceptibility to higher grades of A-V heart block. Established complete heart block, however, is preferable to shifting degrees of block.

The higher grades of A-V heart block are usually chronic and fixed. The routine of the patient should be governed by his general fitness. All those who experience syncopal attacks should be warned of the danger of getting about on their own, because of their susceptibility to syncopal seizures. We have seen such patients who have been treated for years for epilepsy.

The treatment of attacks of Stokes Adams syndrome depends on the underlying mechanism which unfortunately cannot be determined clinically during the attacks, so graphic means must be used. The following measures may be used during the attacks: direct vigorous thumping on the precordium (more likely to be of help in ventricular standstill); intracardiac or intramyocardial injection of adrenalin (for the same type). The occurrence of frequent seizures one following the other, is usually the result of a severe degree of cerebral anoxia, and nearly always indicates a terminal event. We have seen this state improve by oxygen and the intravenous injection of aminophylline. To prevent the Stokes Adams seizures sympathetic stimulants such as ephedrine sulfate 25 mgm., t.i.d., or other sympathicommetic drugs may be given. Thyroid extract and barium chloride have been used. Where these attacks are associated with the prefibrillary type of ventricular tachycardia or ventricular fibrillation quinidine may be given prophylactically. Large doses of papaverine have also been recommended both prophylactically and during attacks.

control of the sinoauricular node. When this is the case some other name (ventricular escape or nodal escape) is given to the disturbance. The A-V node readily takes up the role of pacemaker if either of the following developments takes place: (1) The rhythmicity of the sinoauricular node becomes depressed to a level lower than that inherent in the auriculoventricular node or (2) the rhythmicity inherent in the auriculoventricular node becomes heightened to a point above that of the sinoauricular node. Since the natural rhythmicity of the auriculoventricular node is around 40 to 50 per minute the former development (1) results in a slow heart rate and may be called the slow type of nodal rhythm while the latter (2) produces a rate more rapid than the usual sinus rate and can be referred to as the rapid type of nodal rhythm. Neither type is very common but the slow form is seen more often than the rapid. Both forms of A-V nodal rhythm are nearly always temporary disturbances; only a few instances have been reported where the disturbance approached permanency.

*Etiology.*—A-V nodal rhythm is rare in children. It is observed most frequently in the middle and later decades of life. Among the causes of nodal rhythm are those factors which tend to temporarily inhibit the function of the sinoauricular node or to permanently damage the structure. Vagal stimulation, certain phases of respiration and the initial stage of atropine effect may produce transient periods of nodal rhythm. Injury to the sinoauricular node by toxic processes, myocarditis, especially rheumatic carditis, and degenerative states may result in relatively long periods of nodal rhythm. Digitalis and certain toxic states occasionally produce nodal rhythm when the auriculoventricular rate may be 60 or more per minute.

*Pathology.*—The pathology is that of the conditions described above. The sinus node may be the seat of extensive damage or entirely destroyed by the disease process.

*Symptoms and Signs.*—No symptoms are produced by A-V rhythm itself. The symptoms are those of the underlying cardiac state. Shortness of breath, consciousness of the heart beating slowly, the slow heart rate or irregular heart action are the chief complaints. No signs are observed except a persistent slow pulse which is entirely regular. The rate undergoes slight variations and occasionally marked variations, particularly following exercise or emotion, at which time the auricles and the ventricles beat at a slightly different rate. This also gives rise to variation in the intensity of the first heart sound due to the mechanism described under complete A-V heart block. Not infrequently the premature nodal contractions are associated with and add to the irregularity.

*Diagnosis.*—Although A-V nodal rhythm may be suspected when the apical rate is regular and ranges from 40 to 50 per minute the diagnosis is confirmed chiefly by means of the electrocardiogram. In considering the electrocardiographic diagnosis of A-V nodal rhythm it should be pointed out that the A-V node is a relatively long structure, so much so that the electrocardiographic findings differ depending upon whether the impulses arise in the head or auricular end, in the tail or ventricular end, or in the center. What is seen usually is a migration of the center of impulse formation with some impulses arising from one situation in the node and some from another. Regardless of which center is active there is one common feature: the auricular P waves are inverted or at least different in shape from P waves originating in the sinus node. This is so because an impulse arising in the A-V node follows an entirely different course through the auricular muscle than one arising in the sinus node. The QRS complexes are usually supraventricular, that is, normal in width and shape, though occasionally one sees a slight aberration in the shape of this complex.

When an impulse arises in the ventricular end of the node it has a much shorter distance to go to reach the ventricles than the auricles. Consequently the ventricles are activated and contract before the auricles with the result that inverted P waves are usually situated between the QRS complex and the T wave.

When an impulse arises in the auricular end of the node the distance to be traversed to the auricles is short and the auricles beat

cumbent position Extrasystoles are observed more frequently at slow rates, they are less often observed at high rates Although extrasystoles are usually abolished by exercise there is a small group where they are induced by or are rendered more numerous by exercise This phenomenon is usually observed in hearts which show evidence of myocardial abnormality Extrasystoles that are numerous and arise from different foci are observed in the presence of myocardial damage

*Symptoms* — There may be no symptoms as a result of extrasystoles Frequently however the patient is conscious of what he calls palpitation the heart turns over or the heart stops While in itself this may be of little or no importance the thought that there is something wrong with the heart renders the patient panicky and he feels the imminence of a serious catastrophe Occurring frequently these symptoms arouse intense anxiety on the part of the patient The history frequently given is that they are more troublesome while resting particularly while lying in bed

*Diagnosis* — The interruption of a normal rhythm by premature beats followed by a pause which usually but not invariably is compensatory is a characteristic finding on auscultation These pauses are often difficult to differentiate from those that appear during the Wenckebach phenomenon of partial A-V heart block or the pauses of marked sinus arrhythmia When the period between the extrasystole and the preceding normal beat is short ventricular filling is small and the extrasystolic beat may not be sufficiently strong to open the aortic valve and will therefore fail to produce a palpable pulse at the wrist In these cycles only one sound is heard over the heart The presence of a normal beat followed by an extrasystole repeated in regular sequence is characteristic of coupled rhythm Clinically coupling may be mistaken for alternation of the pulse because of the alternation of weak and strong beats Coupled rhythm is characterized by a rhythmic irregularity consisting of a short pause between the normal beat and the extrasystole and the long compensatory pause following the extrasystole In pulsus alternans the rhythm is quite regular When extrasystoles occur frequently and arise from many different foci the rhythm is indistinguishable clinically from that of auricular fibrillation Most extrasystoles disappear following exercise in occasional cases they become more frequent after exercise This last group is the more serious variety and is the result of myocardial damage The diagnosis of extrasystoles and their exact origin may be determined by the electrocardiogram

*Treatment* — The treatment of extrasystoles is frequently rather unsatisfactory Therapy should be directed to the underlying cause if it can be determined If it is myocardial disease improvement of the heart by rest diuretics, and digitalis may abolish the extrasystoles Gastrointestinal disturbances foci of infection and exogenous poisons should be sought for and removed if possible Frequently the cause cannot be found and in the symptomatic variety the patient should be reassured that they are a normal phenomenon and that they occur frequently in normal hearts If they are frequent and are troublesome to the patient the following therapy is suggested quinidine sulfate 0 2 Gm four or five times daily papaverin 0 06 to 0 2 Gm t i d , potassium acetate, 2 to 4 Gm in a 25 per cent solution of peppermint water every 4 to 6 hours bromides 1 Gm t i d phenobarbital 0 03 Gm t i d Recently procaine amide in doses of 0 25 to 0 5 Gm every 4 to 6 hours has been used in the treatment of ventricular and at times in auricular extrasystoles Psychotherapy is indicated in those cases where emotional conflict may be a factor in the production of the extrasystoles

*Prognosis* — The prognosis depends upon the underlying condition of the myocardium the incidence and grouping of the ectopic beats and the response to therapy

### Auriculoventricular Nodal Rhythm

The term A V nodal rhythm is usually applied when the impulses arising in the A V node either slowly or rapidly spread downward to the ventricles and upward to the auricles and thus control both chambers This is not always the case however for frequently nodal impulses go only to the ventricles while the auricles remain under

control of the sinoauricular node When this is the case some other name (ventricular escape or nodal escape) is given to the disturbance The A V node readily takes up the role of pacemaker if either of the following developments takes place (1) The rhythmicity of the sinoauricular node becomes depressed to a level lower than that inherent in the auriculoventricular node or (2) the rhythmicity inherent in the auriculoventricular node becomes heightened to a point above that of the sinoauricular node Since the natural rhythmicity of the auriculoventricular node is around 40 to 50 per minute the former development (1) results in a slow heart rate and may be called the slow type of nodal rhythm while the latter (2) produces a rate more rapid than the usual sinus rate and can be referred to as the rapid type of nodal rhythm Neither type is very common but the slow form is seen more often than the rapid Both forms of A V nodal rhythm are nearly always temporary disturbances only a few instances have been reported where the disturbance approached permanency

*Etiology* —A V nodal rhythm is rare in children It is observed most frequently in the middle and later decades of life Among the causes of nodal rhythm are those factors which tend to temporarily inhibit the function of the sinoauricular node or to permanently damage the structure Vagal stimulation certain phases of respiration and the initial stage of atropine effect may produce transient periods of nodal rhythm Injury to the sinoauricular node by toxic processes myocarditis especially rheumatic carditis and degenerative states may result in relatively long periods of nodal rhythm Digitalis and certain toxic states occasionally produce nodal rhythm when the auriculoventricular rate may be 60 or more per minute

*Pathology* —The pathology is that of the conditions described above The sinus node may be the seat of extensive damage or entirely destroyed by the disease process

*Symptoms and Signs* —No symptoms are produced by A V rhythm itself The symptoms are those of the underlying cardiac state Shortness of breath consciousness of the heart beating slowly the slow heart rate or irregular heart action are the chief complaints No signs are observed except a persistent slow pulse which is entirely regular The rate undergoes slight variations and occasionally marked variations particularly following exercise or emotion at which time the auricles and the ventricles beat at a slightly different rate This also gives rise to variation in the intensity of the first heart sound due to the mechanism described under complete A V heart block Not infrequently the premature nodal contractions are associated with and add to the irregularity

*Diagnosis* —Although A V nodal rhythm may be suspected when the apical rate is regular and ranges from 40 to 50 per minute the diagnosis is confirmed chiefly by means of the electrocardiogram In considering the electrocardiographic diagnosis of A V nodal rhythm it should be pointed out that the A V node is a relatively long structure so so much so that the electrocardiographic findings differ depending upon whether the impulses arise in the head or auricular end in the tail or ventricular end or in the center What is seen usually is a migration of the center of impulse formation with some impulses arising from one situation in the node and some from another Regardless of which center is active there is one common feature the auricular P waves are inverted or at least different in shape from P waves originating in the sinus node This is so because an impulse arising in the A-V node follows an entirely different course through the auricular muscle than one arising in the sinus node The QRS complexes are usually supraventricular that is normal in width and shape though occasionally one sees a slight aberration in the shape of this complex

When an impulse arises in the ventricular end of the node it has a much shorter distance to go to reach the ventricles than the auricles Consequently the ventricles are activated and contract before the auricles with the result that inverted P waves are usually situated between the QRS complex and the T wave

When an impulse arises in the auricular end of the node the distance to be traversed to the auricles is short and the auricles beat

before the ventricles However, as the impulse is spreading from its point of origin upwards (towards the auricles) it is also spreading towards the ventricle with the result that when the impulse reaches the auricles and the P wave begins to be written, the impulse will be well on its way by then through the node toward the ventricles This naturally results in the P R intervals being quite short

When the impulse arises around the center of the node, it may reach the auricles and ventricles simultaneously, with the result that the QRS complexes and the P waves occur simultaneously and the latter are invisible When this is the case, the diagnosis is *sometimes uncertain and must be arrived* at largely through elimination If one takes enough tracings, usually a cycle or cycles will be found in which the P wave slows, for as we have already stated, the center of impulse formation in the A-V node generally moves and rarely remains fixed However if this does not occur, the following procedures may help

(1) Exercise or atropine may be given to separate the auricular and ventricular rhythms these act by decreasing vagal tone which often affects the sinoauricular node to a greater degree than the A V node

(2) A record of the jugular pulse simultaneously with the electrocardiogram will record an *A* wave occurring synchronously *with the QRS complex*

*A V Nodal Extrasystoles and Nodal Paroxysmal Tachycardia* —A nodal extrasystole is simply a single cycle of rapid type nodal rhythm That is for one cycle the rhythmicity of the A V node is raised to a higher level than that of the sinoauricular node The electrocardiographic features are as previously described inverted P waves either before *behind or buried in the QRS* complexes If before the QRS complexes the P R interval will be shortened If instead of a single isolated nodal extrasystole there occurs a series of these beats this constitutes nodal paroxysmal tachycardia As the name implies it is paroxysmal and the rate may rise as high as 140 to 160 per minute This disturbance is the typical example of the rapid type of nodal *rhythm* but it is quite rare

*Ventricular Escape* —This term applies to those instances in which impulses arising in the A V node go forward and control the ventricle but do not reach the *auricles*, which remain under the control of the sinoauricular node The factors which produce this disturbance and the form in which it manifests itself (slow or rapid) are those already discussed

The "slow" type is easily recognized in the electrocardiogram by the fact that the escaped ventricular complexes are not preceded by P waves The latter can usually be seen at least partially, behind the QRS complexes and can be seen to be normally upright and therefore of sinus origin In the "rapid" type, we have an A-V *dissoci*ation with the ventricles beating more rapidly than the auricles This can be plainly seen in the electrocardiogram by the fact that the ventricular beats are of normal shape but are not preceded by P waves with a constant P-R interval The ventricular complexes are regular in rhythm and are all responses to nodal impulses, except that an occasional beat may be out of rhythm because it is a response to an auricular and not a nodal impulse This can happen when the auricular impulse finds the refractory state of the A-V node and the *ventricles* favorable The P waves are normally upright regular and occur at a slower rate than the ventricular complexes

*Treatment* —If there is an underlying cause such as digitalis it should be removed Any toxic or disease state present should be treated If the condition results from vagal effect, atropine or ephedrine, in doses large enough to produce physiologic effects must be used

*Prognosis* —This depends upon the underlying factors producing the nodal rhythm

## Paroxysmal Ventricular Tachycardia

Paroxysmal ventricular tachycardia is a rather rare but serious type of arrhythmia When a series of six or more ventricular extrasystoles occur in succession they may be said to constitute a paroxysm of ventricular *tachycardia* Its evolution may be observed in serial tracings Occasional ven

tricular extrasystoles initially present are observed to become more numerous and later either coupled rhythm appears or they are observed to occur in sequences of two or three beats. Following this short and then longer paroxysms of ventricular tachycardia may appear. A paroxysm may last a few hours, days or weeks. The danger of this disturbance lies not only in its association with a severely damaged heart and the tendency to exhaustion of the heart muscle but also the predisposal of such rhythm to develop into ventricular fibrillation, a condition practically incompatible with life.

The following types of ventricular tachycardia are observed:

(1) Runs of ventricular extrasystoles all of which have the same configuration with a rate ranging from 130 to 180 per minute.

(2) A bidirectional type of ventricular tachycardia which is usually the result of toxic digitalis effects and which has been regarded by some as a "circus movement" in the ventricles and has been called ventricular flutter. This type is almost always fatal.

(3) A prefibrillary type of ventricular tachycardia which is characterized by extremely bizarre ventricular complexes, the rate of which ranges from 200 to 250 per minute. Such complexes are observed usually immediately preceding or upon emergence from attacks of Stokes-Adams seizures.

*Etiology.*—Paroxysmal ventricular tachycardia almost always occurs in the presence of severe myocardial damage. It is rarely observed in patients where hearts are apparently normal clinically. The following are the most important associations: toxic digitalis effects, myocardial infarction, severe grade of hypertensive and arteriosclerotic heart disease.

*Symptoms and Signs.*—The symptoms of ventricular tachycardia are similar to those of any ectopic rhythm but are apt to be more severe since they are observed in severely damaged hearts.

*Pathology.*—No distinct pathology is observed except that of the underlying conditions mentioned above.

*Diagnosis.*—The diagnosis of paroxysmal ventricular tachycardia is difficult to establish clinically; it can be definitely made by the electrocardiogram. It should be suspected in any instance where the ventricular rate varies from 130 to 180 per minute which does not yield to carotid sinus pressure and there is slight irregularity of the ventricular rate and variation of intensity of the heart sounds because of the superposition of auricular and ventricular contractions at various cycles. The factors in establishing the diagnosis are: the beats of the paroxysms must be ectopic in origin and must conform to those observed as isolated extrasystoles before the onset of the paroxysm; the first beat of the paroxysm must bear the same relation to the preceding normal beat as a coupled extrasystole bears to the preceding normal beat; the ventricles are observed beating regularly at a rate of 130 to 180 per minute and the auricles also beat regularly, slower than and entirely independently of the ventricles. Occasionally ventricular tachycardia is observed in the presence of auricular fibrillation.

The differential diagnosis from the electrocardiographic standpoint involves any ectopic rhythm where the QRS complexes are widened as a result of fatigue of one of the bundle branches incident to the rapid rate. Such widening of the QRS complexes may be observed in auricular tachycardia, auricular flutter and nodal tachycardia.

*Treatment.*—Quinidine is the drug of choice in the treatment of ventricular tachycardia. This may be given by mouth, intramuscularly or intravenously. The dose given by mouth or intramuscularly ranges from 0.2 to 0.3 Gm. four to five times per day. Sometimes larger doses up to 0.6 Gm. per hour are given for 10 or 20 doses. The intramuscular route is used when the patient is in some degree of shock and absorption by mouth may be slow and uncertain. Occasionally quinidine dihydrochloride 0.3 Gm. diluted in 20 to 50 cc. of normal saline is effective when given intravenously. Quinidine acts in stopping a paroxysm of ventricular tachycardia by increasing the refractory period of the ventricle. Other drugs which have been used are potassium chloride 2 Gm. every 2 to 4 hours to supplement or reinforce action of the quinidine; atropine sulfate 2.0 mgm. hypodermically; magnesium sulfate 15 cc. of a 20 per cent

solution, papaverine, 0 2 to 0 3 Gm every 3 hours The treatment by quinidine is effective in about one-half to two thirds of the cases The mistake often made is that the patient is not given enough of this drug

Recently, procaine has been given intravenously to stop paroxysms of ventricular tachycardia with some success Procaine amide has also been used orally in doses of 0 25 to 0 5 gm every 4 to 6 hours or intravenously in doses of from 200 to 1000 mgm Procaine amide is considered by some the drug of choice in the control of ventricular tachycardia The oral dose is 250 mg to 0 5 Gm every 4 hours The intravenous dose is 0 2 to 1 Gm given during a period of 5 to 10 min

*Prognosis* —The prognosis of paroxysmal ventricular tachycardia is extremely serious because it occurs in severely damaged hearts and its duration for a prolonged period predisposes to ventricular fibrillation, a condition which is incompatible with life

### Ventricular Fibrillation

Ventricular fibrillation is the most serious of the arrhythmias its presence is practically incompatible with life Indeed it is often present as a terminal event in dying hearts Comparatively few cases in the human have been recorded by the electrocardiogram These have been obtained when by chance the machine was connected to the patient usually during repeated Stokes Adams attacks In ventricular fibrillation numerous fibrillary impulses traverse the ventricle so rapidly that coordinated contractions do not occur The ventricles are in a continuous state of dilatation similar to that of the auricles in auricular fibrillation The blood pressure drops to zero and unless the mechanism spontaneously changes in a matter of seconds death ensues Electrocardiographic records have been obtained where the patient observed in these seizures spontaneously recovered and the heart returned to a normal ventricular contraction Such instances are rare Patients having developed this mechanism once are subject to repeated attacks so that death is usually not long delayed The etiologic factors associated with this condition have not been established clearly in the human because of the relatively few opportunities to study this condition by reason of its transient nature Many studies have been made in the experimental laboratories with animals and it is believed that the results can largely be applied to man Ventricular fibrillation has been produced by electric shock ligation of the branches of the coronary arteries, by digitalis poisoning and by adrenalin Similar analogous conditions are probably also operative in the production of ventricular fibrillation in the human The myocardial states associated with ventricular tachycardia are probably also a factor in the production of ventricular fibrillation

The diagnosis of ventricular fibrillation cannot be made clinically It is presumed to be present in patients dying from coronary occlusion and digitalis toxicity Its presence is strongly suspected during Stokes-Adams seizures this is particularly so if during the attack the pulse rate previously 20 to 40 per minute jumps to 100 or over per minute (This is usually due to the prefibrillary type of ventricular tachycardia which usually precedes ventricular fibrillation ) In patients subject to attacks quinidine sulfate or procaine amide may be given as a prophylactic measure Administration of epinephrine during a seizure is contraindicated since in itself it may produce ventricular fibrillation and thus may prevent spontaneous recovery Large doses of papaverine have also been recommended for use between and during attacks of ventricular fibrillation Procaine and diethylaminoethanol may also stop a bout of this arrhythmia In occasional cases, electric shock applied to the exposed heart has been effective in restoring a normal rhythm

### Treatment of Rapid Ectopic Rhythms When Exact Diagnosis by Electrocardiogram is Not Available

Not infrequently one encounters patients with rapid heart rates which are the result of an ectopic rhythm These patients are often in a severe state of heart failure and in the absence of an electrocardiogram the

question often arises as to the proper treatment The following summarizes the principles of therapy in those cases

1 Over 90 per cent of ectopic rhythms with rates ranging from 140 to 180 per minute are due to rapid auricular fibrillation auricular tachycardia and auricular flutter

2 These arrhythmias usually respond to digitalis action and its administration may be lifesaving

3 Digitalis is of no value in ventricular tachycardia *it is of course contraindicated* when this tachycardia is the result of toxic digitalis effects

## COR PULMONALE

Cor pulmonale is right sided heart enlargement due to disease in the pulmonary bed right heart failure and tricuspid lesions or congenital defects It is either acute or chronic

### Acute Cor Pulmonale

*Etiology* —Acute cor pulmonale is caused by sudden obstruction of the pulmonary artery or one of its branches usually by a clot Such a clot originates (1) in a leg or pelvic vein (2) in the right side of the heart particularly the right auricle especially when a patient with auricular fibrillation suddenly develops a normal rhythm (3) in the rupture of an aortic aneurysm into the pulmonary artery and (4) in vegetation from an ulcerated pulmonary valve About 60 per cent of the cases of acute cor pulmonale are due to medical causes about 40 per cent to surgical causes Of the medical cases half are due to cardiac causes half to noncardiac causes Chronic heart failure with pulmonary congestion may also result in pulmonary infarcts the so-called autochthonous infarcts

*Pathologic Physiology* —With the lodging of an embolus in the pulmonary artery *there will be a dilatation of the artery distal* to the embolus and a dilatation of the right ventricle The thrombus may become more or less organized if the patient survives for some period of time The lung area involved *by the thrombus shows* hemorrhagic infarction usually surrounded by an area of pneumonitis This area of hemorrhagic infarction may develop infection and abscess formation The presence of the thrombus throws an increasing strain on the right ventricle so that it gradually dilates There will also be diminished aeration of the blood sent to the lung because there is less functioning pulmonary tissue A spasm of the coronary artery will also result this is due to the so-called pulmonocoronary reflex In addition to that all the other pulmonary vessels will suffer spasm this will throw still *greater strain* upon the right side of the heart

*Signs and Symptoms* —The symptoms of pulmonary embolism depend on the site of the involvement and the size of the vessel occluded In the typical surgical case the *embolus occurs from 10 to 14 days after* abdominal or pelvic surgery or after childbirth The victim is seized with a sudden agonizing pain or oppression in the substernal region accompanied by the symptoms of shock this either while he is lying quietly or just after he attempts to sit up Death may be instantaneous Pallor and profuse sweating accompanied by a low blood pressure and a rapid pulse may occur Cough and hemoptysis are usually but not invariably present If the embolus is small the symptoms may be slight In many cases of pulmonary embolism the above mentioned symptoms are absent or so mild as to pass unnoticed even when the embolus is of fair size At times, there may even be multiple small emboli with a minimum of signs or symptoms These cases will often simulate a mild pneumonitis *In addition to* dyspnea and cyanosis and a shock like picture the heart rate is rapid and the pulmonic second sound is accentuated One may also hear a systolic murmur over the pulmonic area *There will be increased pulsation in the* second and third interspace to the left of the sternum The blood pressure is low and during the first twenty four hours no pulmonary signs may be observed Thereafter *two types of pulmonary findings* may appear In one type there is evidence of congestion of a localized area of the lung usually the right base In the other type there is a wedge shaped triangular area of congestion In some cases though it is not common in addition to the above findings, one may note jaundice

*X-ray Findings.*—The x-ray signs do not ordinarily appear for from 24 to 36 hours. Usually they consist of an area of pneumonitis like congestion at the right base or (more rarely) a triangular area of consolidation. In doubtful cases, one may use angiocardiography to demonstrate the obstructed pulmonary-artery branch and so confirm the diagnosis.

*Electrocardiogram.*—The electrocardiogram is not pathognomonic in the diagnosis of pulmonary infarction, though it may be a help when serial tracings are taken. The findings depend upon the presence of right ventricular strain and anoxia. In the characteristic case one will find a deep S wave in lead I, a low to inverted T wave in lead II, a Q wave in lead III, and a deeply inverted T wave in lead III. Furthermore the RT segment in lead III may be elevated, the T wave in the precordial leads is flattened or inverted, the RT segment may be depressed and the QT interval may be prolonged. There may also be a delay in the onset of the intrinsicoid deflection in leads over the right precordium and the right ventricular pattern may be noted far over to the left in the precordial leads. Occasionally transient right bundle branch block may be observed.

*Differential Diagnosis.*—Acute cor pulmonale must principally be distinguished from coronary occlusion. A history of recent operation, findings of right ventricular strain, evidence of pulmonary infarction and absence of characteristic electrocardiographic evidence of coronary occlusion speak for pulmonary embolism. Acute cor pulmonale must also be differentiated from dissecting aneurysm of the aorta and spontaneous pneumothorax. The development of a spontaneous mediastinal emphysema may also be mistaken for acute cor pulmonale, but if the so called "crunch" sound over the heart in systole is present, the condition is not cor pulmonale.

*Treatment.*—Treatment against the development of pulmonary emboli is becoming more and more common. Early ambulation of surgical patients has reduced the incidence of phlebothrombosis of the leg, and medical patients who may be expected to develop emboli are now treated prophylactically with such agents as heparin, dicumarol and other anticoagulants. This is routine for patients who have had coronary occlusion or have auricular fibrillation and have already suffered one pulmonary embolus. Furthermore, before an attempt is made to restore an auricular fibrillation of some standing to a regular sinus rhythm, it is recommended that the patient be prophylactically treated with anticoagulants.

Once a pulmonary embolism has occurred the patient should be put to bed and given oxygen, as well as morphine and atropine. Papaverine in doses of from 0.06 to 0.12 Gm. should be given intravenously at 2 to 4 hour intervals in an attempt to overcome vascular spasm. In addition the patient should be heparinized at once and then given dicumarol to prevent further embolization. In some clinics, it is also the custom to ligate any peripheral veins which have been found to contain thrombus formation. But the value of this procedure is now seriously questioned.

Stellate block has also been used to treat the acute episode of pulmonary embolism. This procedure acts by preventing reflex vascular spasm, thereby reducing the strain on the right side of the heart.

## Chronic Cor Pulmonale

*Etiology.*—Chronic cor pulmonale is gradual in development and permits the right side of the heart to adjust itself to the enlargement.

Left heart failure is a common cause of chronic cor pulmonale, for as the left side of the heart fails, pulmonary congestion develops and throws an extra load upon the right ventricle and hypertrophy results. Mitral stenosis is also a common cause of chronic cor pulmonale, for back pressure from the left auricle into the lungs results in pulmonary congestion and right ventricular strain follows. Furthermore, in rheumatic heart disease, the common cause of mitral stenosis, the elasticity of the lung is reduced and pulmonary endarteritis develops. Both of these factors result in right ventricular strain because it elevates the pulmonary pressure by raising resistance to the flow of the blood through the lungs. This increased

resistance results from the widespread destruction of the interalveolar septa and the findings of one usually accompany evidences of the other

The *principal manifestations* of right sided heart failure are cyanosis polycythemia clubbing of the fingers engorgement of the superficial veins increased venous pressure swelling and tenderness of the liver (and occasionally of the spleen) edema of the legs transudations into the serous cavities, eventual dilatation of the right ventricle and right auricle and tricuspid insufficiency (as evidenced by a systolic murmur and accentuation of the second pulmonic sound) Occasionally a diastolic pulmonary murmur may be heard the result of a relative insufficiency of the pulmonary valve so-called right sided gallop rhythm may be heard at times Oliguria as well as a rise in cerebrospinal fluid pressure may be observed too The dyspnea present varies in intensity The circulation time is usually not altered in early cases of chronic cor pulmonale but is increased when heart failure occurs

*X ray Findings* —In long standing cases the x ray shows enlargement of the right auricle particularly with the onset of the right heart failure Enlargement of the pulmonary artery, with increased pulsation of that artery is a characteristic finding In the posteroanterior view of the heart one of the first signs of right sided heart enlargement may be a prominence of the pulmonary artery segment and in the right anterior oblique position enlargement of the right ventricle as well as of the pulmonary artery will be seen The lung fields will be clear in pure right sided heart failure though if left sided heart failure has preceded it there will be evidences of pulmonary congestion

*Electrocardiographic Findings* —The electrocardiogram usually shows a right axis deviation In the precordial leads there are evidences of right ventricular hypertrophy and these findings are borne out in the unipolar leads There may be broad notched P waves and right bundle branch block is a common finding There is delay in onset of the intrinsicoid deflection in right precordial leads and the right ventricular pattern may be seen in the 4 5 and even 6 positions over the precordium Auricular fibrillation is a common arrhythmia in chronic cor pulmonale

*Course* —The onset of chronic cor pulmonale is insidious Heart failure may not occur for many years Acute pulmonary infections superadded to lung disease already present may cause sudden death Congestive heart failure rarely causes death in patients with pure right sided heart failure unless pulmonary arteriosclerotic changes take place then death comes quickly once cyanosis has developed

*Treatment* —The treatment of this condition consists in correcting the underlying pulmonary disease or other conditions putting strain on the right side of the heart In most cases this is hard to do But the antibiotics and new procedures in pulmonary surgery have made it easier The treatment of right sided heart failure is like that for congestive failure

The use of oxygen however presents certain hazards Patients with chronic cor pulmonale have so high a carbon dioxide level in the blood that carbon dioxide fails to stimulate their respiration Their only stimulus to respiration then is the low oxygen tension If these patients are placed in an atmosphere of 100 per cent oxygen the stimulus to respiration may cease and the patient die It is therefore wise to use oxygen mixtures for these patients or keep them in 100 per cent oxygen only intermittently for periods of from 15 to 20 minutes till there is re-establishment of the carbon dioxide stimulus to respiration

Change of climate may also be helpful in these cases by helping prevent secondary pulmonary infection Such cases do best in temperate climates and low altitudes

## THE TREATMENT OF HEART FAILURE

There are several classifications of heart failure The discussion here is limited to some of the more important types *Low output failure* is seen in hypertension stenosis of the aortic and mitral valves coronary atherosclerosis and myocarditis either degenerative or inflammatory Here there is

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### TREATMENT OF EDEMA

*Diuretics* — The use of the mercurial diuretics is probably the most important single method employed in treating the edema of heart failure. These agents prevent the reabsorption of sodium by the renal tubule. Considerable amounts of sodium are therefore eliminated in the urine and large amounts of water are carried with this electrolyte. The diuretic may be given intravenously, subcutaneously, intramuscularly, orally or rectally.

Relatively few contraindications to the administration of the mercurial diuretics exist. They may be given even when albumin is present in the urine or a mild or moderate azotemia exists. The chief contraindications to their use are acute glomerulonephritis and marked azotemia of renal origin.

The patient should be weighed upon admission to the hospital, or when first seen by the physician, and daily during the administration of the diuretic. The frequency of administration of mercurial diuretics in the initial stages of congestive heart failure is as follows: initial dosage—0.5 to 1.0 cc subcutaneously or intramuscularly repeated daily or increased to 2.0 cc until a considerable amount of fluid is removed; subsequent dosage—1.0 to 2.0 cc every other day or every third day until most of the extracellular fluid has been removed (patient will fail to lose more weight after an injection of the diuretic—so called dry weight), then it should be given every one or two weeks or oftener as indicated by patient's weight, symptoms and signs. Mercurial diuretics sometimes have untoward effects. Sudden death has been reported following the administration of such diuretics. In older patients, especially in hot weather, the mercurial diuretics must be used with caution since in these patients such diuretics may cause weakness, apathy, leg cramps, a shock like state and even death. These episodes may be *observed* as the result of the loss of electrolytes, especially chloride and sodium and occasionally *calcium*. Such untoward effects may be prevented by the administration of smaller doses of the mercurials, the administration of salt before and after the administration of these diuretics, and observation of the level of serum sodium, especially in patients on a sodium poor diet. Calcium may prevent leg cramps in some patients and quinine in others.

Coronary occlusion has also followed the administration of the mercurials. Occasionally patients develop extrasystoles as a result of having been given mercurial diuretics. Fatal arrythmias have also occurred. It is believed that digitalization before administration of a mercurial diuretic results in extrasystoles because of a redigitalization due to the action of the glycoside in the reabsorbed extracellular fluid.

Occasional instances of renal shut down with intractable anuria have apparently resulted from the administration of mercurial diuretics, even though it has been proved that they will in themselves not produce kidney pathology.

Deficiencies of the water soluble vitamins may also result from the administration of these diuretics.

Patients who have received the mercurial diuretics with good response over a period of months or years sometimes reach a point at which they no longer respond to them. The treatment of such mercurial fast patients involves a rather serious problem. First one should differentiate such cases from cases of oliguria due to mechanical factors, such as the presence of ascites and/or a fall in blood pressure with decreased renal blood flow. By removing the mechanical factors, such as the ascitic fluid or by restoring the blood pressure to a more normal level, diuresis may again be established. If the patient becomes mercurial fast, the following must be considered: (1) inadequate digitalization (if the patient is not adequately digitalized, this may be a factor and should be corrected), (2) over digitalization (this too may be a factor in preventing proper utilization of the mercurial diuretics), (3) hypochloremic alkalosis (when the chloride level drops below 86 mEq the patient will become refractory to the mercurial diuretics and one must then give ammonium chloride orally or intravenously, though the latter method is somewhat dangerous), (4) hyponatremia (sodium

an increase in venous pressure, and the work of the heart is increased to a point at which the heart goes into failure and its output drops In *high-output failure,* the cardiac output is initially high and often associated with an increase in the circulating blood volume It is seen in severe anemias, emphysema, chronic cor pulmonale, thyrotoxicosis beriberi heart disease, arteriovenous aneurysms, pregnancy, osteitis deformans interauricular septal defect, and in neuroses associated with increased metabolic rates with increased demands on the heart Here in the presence of heart failure the cardiac output remains high

In *left-sided heart failure* the manifestations consist of pulmonary congestion and pleural effusion In *right-sided heart failure* there is evidence of congestion of the liver increased venous pressure, ascites, and edema of the lower extremities

*Methods of Treatment* —The treatment of heart failure may be discussed under the following (1) rest of the heart (2) cardiac edema (3) acute heart failure (4) surgery, (5) additional measures

### *Decrease of Cardiac Work*

*Bed Rest* —The importance of bed rest in the treatment of heart failure cannot be overemphasized Bed rest not only reduces the work of the heart to a minimum but decreases the metabolic demands of the tissues for blood Bed rest is not nearly so important, however in cases of left heart failure as in cases of right heart failure In left heart failure the periods of bed rest may sometimes be curtailed to about one or two days Then if the patient sits up fluid will gravitate to the lower portions of the body and diminish the strain on the heart In right heart failure bed rest may be prolonged to two or three weeks If bed rest is too prolonged especially if the patient is old, hypostatic congestion of the lungs followed by pneumonia, phlebothrombosis with pulmonary infarction or (though seldom) arterial thrombosis may develop furthermore decalcification of bone and urinary difficulties may also occur Patients over fifty or with a tendency to phlebothrombosis should be encouraged to exercise their arms and legs and move about in bed as much as possible, and they should be allowed to get up as soon as their condition permits The use of anticoagulants as a prophylactic measure against the development of vascular occlusion in such patients particularly in those with auricular fibrillation is gaining popularity rapidly

*Low Calorie Diet* —A diet containing from 800 to 1000 calories reduces the work of the heart by reducing the metabolic rate which may drop to minus 20 or minus 30 per cent Weight loss, especially in the obese patient, is also important, since bringing the weight down to the optimal range may not only improve the exercise powers of the heart but postpone for years the onset of heart failure obesity strains the heart by increasing metabolic demands and causing fatty changes in the heart which are deleterious to the optimum function of that organ

*Drugs for Lowering Metabolism* —The introduction of such drugs as propylthiouracil and methylthiouracil, drugs capable of reducing the basal metabolic rate, have also been used in attempts to lower the demands of the body upon the heart Propyl thiouracil in doses of 100 mg given every 8 hours has been used not only for patients with thyrotoxicosis but also for patients with heart failure unassociated with thyroid disease The exact status of this method of treatment is not yet certain

*Treatment of Rapid Rate* —The occurrence of an arrhythmia with a rapid ventricular rate results in myocardial exhaustion due to abbreviation of the diastolic rest period of the heart This condition may even produce heart failure in the normal heart A rapid ventricular rate associated with auricular flutter or auricular fibrillation responds to digitalis Paroxysmal auricular tachycardia may be abolished by carotid-sinus pressure by the administration of prostigmine plus carotid sinus pressure by digitalization or by the administration of quinidine Nodal tachycardia yields to similar therapeutic measures Ventricular tachycardia can usually be abolished with quinidine or pronestyl (*see* section on the treatment of arrhythmias)

help the heart and enable diuretics and digitalis to act more efficiently. Pericardial effusions resulting from congestive heart failure are usually not large enough to require paracentesis. But where pericardial effusions are great and heart failure results it is advisable to remove the effusion in order to increase cardiac efficiency. In the occasional patient with marked edema of the extremities Southey tubes may be used to help drain off the excess fluid.

### Digitalis in Heart Failure

*Preparation and Dosage.*—Many preparations of digitalis drugs and their glycosides are available for the treatment of heart failure. The type of preparation used depends on the individual preference and the mode of administration. The drug may be given orally, intravenously or intramuscularly, the first being the most popular. The following preparations are commonly used if the drug is given orally: the powdered leaf, digitoxin, digoxin, digilanid, lanatoside C and cedilanid. The following table lists the drugs, the amount commonly required for full digitalizing dose and recommended daily maintenance dose.

The initial digitalizing dose is that recommended for a patient weighing 150 pounds (about 70 kilos); however, the dose required for full digitalization varies considerably with the patient. Sometimes twice the recommended dose is required or even more. Although the recommended digitalizing dose is sometimes administered all at one time, it is best to give half the dose initially and the other half in two doses at twelve-hour intervals. Toxic effects rarely occur with the lower digitalizing dose mentioned. They not infrequently occur with higher doses.

| *Drug* | *Full Digitalization Dose by Vein* | *Full Digitalization Dose by Mouth* | *Daily Maintenance Dose* |
|---|---|---|---|
| Digitalis leaf | 3-5 cat units (Digalin) | 15 cat units (22 1/2 gr.) | 1/2 to 1 cat unit |
| Digilanid | 3.0 mg. | 15 cat units (3.0-8.0 mg.) | 0.3 mg. |
| Digitoxin | 1.25 mg. | 1.2 to 3.6 mg. | 0.05 to 0.2 mg. |
| Digoxin | 1.2 mg. | 2 to 5 mg. | 0.25 to 0.75 mg. |
| Gitalin | — | 6.5 mg. | 0.25 to 0.75 mg. |
| Cedilanid (Lanatoside C) | 1.6 mg. | 5 to 10 mg. | 0.5 to 1.2 mg. |
| Oubain | 0.7-1.0 mg. | — | — |
| Strophanthin | 0.7-1.0 mg. | — | — |
| Strophoside | 1.0 mg. | — | — |
| Scillaren | 1.0-1.75 mg. | 9-14 mg. | 0.8-1.6 mg. |

Summary of Effects and Doses of Digitoxin, Digoxin and Lanatoside C

| | *Digoxin* | *Digitoxin* | *Lanatoside C* |
|---|---|---|---|
| Daily undivided dose most likely resulting in maintenance | 0.5 mg. | 0.1 mg. | 1.0 mg. |
| Daily undivided dose most likely resulting in toxicity | 1.0 mg. | 0.2-0.3 mg. | 1.5-2.0 mg. |
| Ease of achieving maintenance | Good | Good | Fair |
| Ease of predicting dose | Good | Good | Trial and error |
| Dissipation | Rapid | Slow | Rapid |
| Duration of toxicity | Short | Long | Short |

Speed of Action of Digitalis Preparations Given Intravenously

| | *Action Starts* | *Full Effect* |
|---|---|---|
| Ouabain | Few minutes | 1 hour |
| Cedilanid | 15-30 minutes | 2 hours |
| Digilanid | 3 hours | — |
| Digitoxin | 3 hours | 6 hours |

chloride may be administered in order to correct this condition) (5) In some patients the administration of 10 per cent glucose is also helpful and in others the administration of aminophylline or decholin before the diuretic is very helpful in restoring the effectiveness of the mercurial (6) Peritoneal lavage has been recommended but this is a rather dangerous procedure It should be used only as a last resort It is important to remember that, if several doses of the mercurial diuretic have been given and no diuresis has been obtained it is usually dangerous to administer the drug further for its retention in the body may produce toxic mercurial symptoms

*Other Diuretics* —Other diuretics may be used alone or as an adjuvant to therapy with the mercurials Ammonium chloride 3 to 8 grams a day, may be used but it is usually not necessary The xanthine group of drugs is occasionally used for diuretic effect however, they rarely by themselves suffice in the treatment of congestive heart failure If used they may be given as theobromine sodium acetate 0 5 grams three times a day or theophylline ethylene diamine 0 5 gram three to five times a day or theobromine calcium salicylate 0 5 grams three to five times daily Urea in a dose of 20 grams, may be administered from 2 to 5 times a day Because it is difficult to take by itself it is usually given with fruit juices iced fluids, or syrup

*Dietary Regimen —Salt and Water Intake* —A salt poor diet low in calories is preferred during the initial stage of heart failure For this purpose, the Karrell diet may be used This consists of 1000 cc of milk a day the milk contains 1 gram of salt The patient is put on this diet for a few days or a week, after satisfactory diuresis has resulted the caloric content of the diet may be raised and further foods added The fluid intake may then be increased to from 2000 to 3000 cc a day and the salt intake to 2 grams The importance of a salt poor diet cannot be overemphasized The normal daily diet contains about 10 grams of salt Patients with heart failure can eliminate only about 2 or 3 grams of salt a day The usual salt poor diets contain 5 or 6 grams of salt The salt which cannot be eliminated is retained in the body and produces edema The best way is to keep a patient on a dietary regimen of about 1½ grams of salt a day is to examine every dietary item to be given that patient and make sure that it is salt free Even salt free bread may be obtained Salt substitutes may be used to make the diet more palatable There are a number of such substances available such as neo curtisal diasal and chlor salt On the type of low-sodium diet described here, the patient may take fluids up to 3000 or 4000 cc a day without danger of water retention The water intake should be approximately 1 0 or 1 5 cc for each calorie ingested If the water intake is inadequate casts albumin and red blood cells will appear in the urine and the urea nitrogen level will rise It is therefore essential that the water intake be adequate and the sodium as low as possible

*Cation Exchange Resins* —Recently cation-exchange resins have been developed in an effort to reduce sodium retention without forcing the patient to live on an unpalatable diet These resins are insoluble acids capable of removing basic ions from solutions with which they come in contact Exchange resins have the disadvantage however of causing gastrointestinal irritation acidosis and depletion of potassium calcium and magnesium But the gastric irritations may be decreased by using carboxylic instead of sulfonic types of resins and ammonium instead of hydrogen exchangers Further if potassium is added to the resins the danger of potassium depletion is minimized

These exchange resins by absorbing sodium from the gastrointestinal tract and carrying it in to the feces permit the patient to have more sodium in his diet Nevertheless the patient with heart failure must not have more than 3 to 5 grams of sodium a day even though he is taking such a resin The usual dose of the carboxylic resin with potassium is 15 grams 3 or 4 times daily The dosage of course often needs adjustment in the individual case Further to be certain that complications from electrolyte deficiencies do not occur electrolyte studies must be performed at regular intervals

*Removal of Effusions* —Removal of pleural effusions and ascitic fluid may indirectly

help the heart and enable diuretics and digitalis to act more efficiently. Pericardial effusions resulting from congestive heart failure are usually not large enough to require paracentesis. But where pericardial effusions are great and heart failure results it is advisable to remove the effusion in order to increase cardiac efficiency. In the occasional patient with marked edema of the extremities Southey tubes may be used to help drain off the excess fluid.

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The following patients develop toxic effects on the smaller dose and should be given digitalis with care: patients with aortic stenosis, those manifesting a severe grade of myocardial damage, those with overactive vagal tone, those in the older age group, and those having a fresh myocardial infarction.

The maintenance dose of the digitalis drugs also varies considerably in different patients and at different times in the same patient. It is suggested that after digitalization the average dose for maintenance be given the patient. The patient should not be kept on this dose indefinitely but should be frequently checked up on and the dose increased or decreased, depending on the patient's need and response.

Recently, the trend has been to administer the pure glycosides, such as digitoxin, digoxin, cedilanid, and lanatoside C, or a combination of these glycosides, such as digilanid, rather than the powdered leaf. The advantages of this are the smaller required dosage, the greater accuracy in standardizing the drug, and the absence of local irritating effects on the gastrointestinal tract. The action of these purified preparations, however, is not always exactly the same as that of the powdered leaf. The purified preparations vary in the degree of muscular and vagal effect they have, and the dosages, even for patients with auricular fibrillation, are difficult to compare with those of the powdered leaf. But by digitalizing the patient as outlined and by giving an adequate maintenance dose and observing the patient for the desired as well as toxic effects, almost any of these preparations can be used successfully.

*Parenteral Administration.*—The intravenous administration of digitalis drugs is indicated when the maintenance of a rapid effect is mandatory and oral administration is considered slow and undependable, as for example in severe cases of advanced heart failure after the occurrence of rapid auricular fibrillation or flutter. In some of these cases intravenous administration of the drug has dramatic and almost immediate effects. An effect from strophanthin may be obtained as early as five minutes after administration. It is important to remember, however, that, if the intravenous route is used, the danger of toxicity is increased. This route should not be used if the patient has received digitalis during the previous two weeks. It is safest to administer half the intravenous digitalizing dose and wait half an hour or an hour, in order to note the effect of the initial dose; additional doses may then be given either orally or intramuscularly, which is much safer. Ouabain, strophanthin and cedilanid not only act rapidly but are dissipated rapidly, so that, after the full effect is obtained, digitalization by mouth may be begun.

The intramuscular route is also indicated if the need for haste is not so urgent as that mentioned above but relatively rapid and dependable absorption of the drug desired.

*Tolerance.*—The tolerance for digitalis varies considerably with the age of the patient, the type and severity of the heart condition, and the absence or presence of heart failure. In general it may be said that older patients and those with greatly damaged hearts show decreased tolerance to digitalis and manifest a very narrow range between therapeutic and toxic effects. In such patients, toxic effects may occur long before maximum therapeutic effects appear. Patients with acute myocardial infarction apparently cannot tolerate the same amount of the drug as other heart patients. Patients with partial A-V block and those with aortic stenosis are apparently more susceptible to the development of increasing degrees of heart block on relatively small doses of the drug. In some cases of partial auriculoventricular block, however, the use of digitalis has so improved the myocardial efficiency that the block disappears entirely when the heart failure disappears. This, though, is rather rare.

*Toxicity.*—The most important symptoms of the untoward effects of digitalis are malaise, headache, anorexia, nausea, vomiting, diarrhea, and occasionally psychoses and eye symptoms. The initial symptoms—malaise, headache, and anorexia—may be obscured by the underlying cardiac state, but nausea and vomiting are fairly dependable signs of toxic effect. It is well to remember, though, that when the powdered leaf is given, nausea and vomiting may result from a local irritating effect of the drug on

the gastric mucous membrane When this is the case purified preparations are administered It should be emphasized that vomiting is not invariably present with digitalis toxicity The electrocardiogram may show extremely dangerous evidence of such toxicity though neither nausea nor vomiting has occurred This is especially true in advanced cases of heart disease and in senile patients In such cases marked weakness and asthenia with clear-cut evidence of toxicity as shown by dangerous cardiac irregularities often occur instead of nausea and vomiting The cardiac manifestations are often more dependable signs of *digitalis toxicity than vomiting or diarrhea*

Though as stated above the vomiting produced by digitalis may be due to local irritation of the mucosa of the gastrointestinal tract a more common cause of it is the action of the drug on the medulla where there is an increase in irritability This increase in irritability of the medulla makes the 'vomiting center' respond to stimuli which might otherwise be of no significance The diarrhea produced by digitalis overdosage is also more often a central nervous system phenomenon than the result of local irritation Psychoses observed in cases of digitalis toxicity are apparently due to a concommitant cerebral circulatory disturbance rather than to a direct effect of the drug but this has not been finally decided Eye symptoms—spots and various colors such as green blue and yellow before the eyes—are often occasioned by digitalis toxicity but these are usually temporary and disappear with discontinuance of the drug These eye findings are believed to result from direct toxic effects of the drug on the primary optic centers in the brain Digitalis should be stopped when (1) the heart rate drops to 60 or below (2) a regular pulse becomes irregular (3) a bigeminal rhythm develops or (4) the cardiac rate previously between 80 and 100 suddenly becomes rapid or rapid and irregular with a rate of from 140 to 180 beats a minute

The electrocardiographic evidence of digitalis effects consists of characteristic alterations of the T waves and the ST segments The ST segments in leads 1 2 and 3 and the precordial leads are depressed and show a bowing or sagging with the concavity upward This bowing may drop the ST segments several millimeters below the base line This may then cause the T waves to be diphasic or even inverted Often however the T waves will show only flattening The PR interval becomes prolonged and heart block of various grades may result In some electrocardiograms, several of these evidences of the drug's action may be observed in one tracing Most of these electrocardiographic alterations are likely to occur within the therapeutic range of digitalis action The presence of the following however, are *unequivocal signs of toxicity* (1) high-grade A-V heart block becoming complete heart block, (2) A V dissociation with ventricular escape (3) numerous ventricular extrasystoles (4) coupled rhythm (5) auricular tachycardia with A-V heart block and (6) ventricular tachycardia The treatment of these ectopic rhythms consists in stopping the digitalis Quinidine and procaine amide may be of help in correcting the ventricular extrasystoles coupled rhythms, and ventricular tachycardias

*Treatment of Acute Left Heart Failure* —In treating acute left heart failure the underlying heart condition (such as coronary artery disease aortic or mitral valvular disease or hypertension) must be corrected certain reflexes must be abolished rapid ectopic rhythms (which may have precipitated the attack) must be eliminated and the circulating blood volume must be decreased so that the damaged heart can work with less strain

(*a*) *Treatment During Attack* —During the attack the patient is usually much more comfortable in a sitting or upright position The initial therapeutic procedure is the administration of morphine sulphate, 15 mgm given alone or with atropine 0 4 to 0 8 mgm The morphine sulphate may be given subcutaneously intramuscularly, and at times (during a shock like state) intravenously The earlier this is given after the beginning of an attack the better the therapeutic result will be In many patients administration of this drug alone will abort the attack in 10 or 15 minutes In older patients who are sensitive to the effects of morphine the

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some of them offer a certain degree of hope An operation to diminish the strain on the left auricle consists in anastomosing one branch of the pulmonary vein to the azygous vein This results in a short-circuiting of some of the blood from the left auricle to the systemic venous circulation It results, in effect in a recirculation of blood but though it may partially reduce the strain on the left auricle it is doubtful whether this is the final answer to the problem

*Adherent Pericardium in Constrictive Pericarditis* —Adherent pericardium in constrictive pericarditis may result in heart failure (and failure of diastolic filling) Removal of the adhesions around the body of the heart and inferior vena cava has resulted in some cases in cure of the heart failure When this is the cause the treatment may produce miraculous results

*Supplementary Therapeutic Measures* —*Nutrition* — Poor nutritional states may aggravate at times, and precipitate heart failure The correction of such states is advised by dietotherapy treatment for anemia or the use of blood and plasma

*Chemotherapy and Antibiotics* — Infectious states may also aggravate or precipitate heart failure These states may be treated with chemotherapeutic and antibiotic agents The prophylactic use of sulfonamides and penicillin in rheumatic carditis will help prevent heart failure

*Treatment of Metabolic Disorders* —The adequate treatment of diabetes particularly the coma and the acidosis is important since the coma and the acidosis of diabetes have deleterious effects on the heart also uncontrolled diabetes hastens the development of arteriosclerosis

*Treatment of Electrolyte Changes* —Alterations in the electrolytes are observed in a variety of conditions as in inanition after surgery vomiting and diarrhea in renal disease and in various metabolic disorders The effects of a low serum sodium level have already been discussed Hypocalcemia increases the irritability of the heart muscle A low serum potassium level results in a disturbance of the function of the already diseased heart Patients with heart failure who respond poorly to the usual therapy will show improvement when the electrolyte picture is corrected

*Climate* —Patients subject to congestive heart failure do best in a mild climate They do not do well in hot weather this is probably the result of an increase in cardiac output loss of electrolytes and excessive thirst with difficult elimination of water Air conditioning in hot weather greatly helps such patients Cold weather also increases the work of the heart especially by increasing peripheral resistance and so may precipitate a bout of congestive failure

## REFERENCES


*General Textbooks of Cardiology and Physiology*

BEST C H and TAYLOR N B The Physiological Basis of Medical Practice 5th ed Baltimore The Williams & Wilkins Co 1950

FRIEDBERG CHARLES K Diseases of the Heart Philadelphia W B Saunders Co 1949

FULTON J F A Textbook of Physiology 16th ed Philadelphia W B Saunders Co 1949

GOLDBERGER E Heart Disease Its Diagnosis and Treatment Philadelphia Lea & Febiger 1951

New York Heart Association Nomenclature and Criteria for Diagnosis of Diseases of the Heart New York J J Little and Ives Co 1943

STROUD W D Diagnosis and Treatment of Cardiovascular Disease 4th ed Philadelphia F A Davis Co 1950

WHITE PAUL D Heart Disease 3rd ed New York The Macmillan Co 1944

WIGGERS CARL J Physiology in Health and Disease 5th ed Philadelphia Lea & Febiger 1949

*Methods of Examination*

COURNAND A BALDWIN J S and HIMMELSTEIN A Cardiac Catheterization in Congenital Heart Disease New York The Commonwealth Fund 1949

DOCK W and TAUBMAN F Some Technics for Recording the Ballistocardiogram Directly from the Body Am J Med 1949 7 751

KATZ L N Electrocardiography 2nd ed Lea & Febiger Philadelphia 1946

PULLEN R L Medical Diagnosis Applied Physical Diagnosis Philadelphia W B Saunders Co 1945

SCHWEDEL J B Clinical Roentgenology of the Heart New York Paul B Hoeber Inc 1946

STARR I and SCHROEDER H A Ballistocardiogram Normal Standards Abnormalities Commonly Found in Diseases of the Heart and Circulation and Their Significance J Clin Invest 1940 *19* 437

respirations may drop to 10 or less a minute In such patients it is well to administer with the morphine a respiratory stimulant such as caffeine coramine or metrazol Digitalization if the patient has not had any digitalis for two weeks or more, may be accomplished rapidly by intravenous administration of strophanthin 0 6 to 1 2 mgm or cedilanid, 0 8 to 1 6 mg If less haste is required, digalin may be given intramuscularly in a dose of from 3 to 5 cat units Generally however digitalization is less efficacious than the other procedures mentioned for the treatment of the acute attack

Caffeine with sodium benzoate 0 5 grams may be given initially and repeated every 2 or 3 hours for about 3 doses This acts as a respiratory and cardiac stimulant Coramine 1 cc may be repeated 2 or 3 times over a period of 2 or 3 hours Aminophylline 0 3 gram may be given slowly intravenously in a 200 cc drip of 5 per cent glucose and may be repeated in about one hour The beneficial effects of this drug depend on its action as a respiratory stimulant and, possibly as a coronary dilator

Oxygen may be given by nasal catheter mask or tent it may be necessary to give it under positive pressure The administration of oxygen is very important in left heart failure since the heart suffers five times as much from lack of oxygen as does skeletal muscle The maintenance of the maximum degree of oxygenation is important for the optimum function of the heart particularly when the pulmonary vascular field available for oxygenation is diminished as it is in left heart failure

In the plethoric patient with distended veins, venesection of from 250 to 500 cc of blood is of help in rapidly reducing the strain on the left side of the heart This should not be done if the patient is asthenic has experienced frequent attacks of heart failure is anemic or does not have distended veins A bloodless venesection may be accomplished by the application of tourniquets to all four extremities These should be tight enough to prevent venous return but not tight enough to prevent the inflow of arterial blood These may be kept on for 10 or 15 minutes then one extremity at a time is released in rotation This regimen is of as much help in reducing the circulating blood volume as is venesection Though the administration of 50 per cent glucose or sucrose has been recommended for the treatment of pulmonary edema, because of their osmotic effect it is not considered a safe procedure

After the attack of left heart failure the patient should be kept at rest in bed for one or two days Frequently, the patient feels quite well the morning after the attack and is often able to go about his work It is advisable however, to watch such a patient for he may develop a mild bronchopneumonia This usually yields to the antibiotics

(b) *Prophylactic Measures in Patients Subject to Attacks of Left Heart Failure* —The following measures will help prevent recurrent attacks of left heart failure (1) bed rest (2) restriction of sodium intake and correction of fluid intake, (3) digitalization, (4) administration of mercurial diuretics (one injection every week or two or more frequently as indicated by the patient s weight-curve and clinical signs and symptoms as previously outlined these diuretics may be given with or without ammonium chloride two or three grams a day (5) light supper with little fluid before bedtime instead of heavy meals (6) raising the head of the patient s bed 8 or 9 inches from the floor (7) administration of aminophylline 0 2 grams 3 times a day by mouth and/or 0 67 grams rectally at bedtime (other drugs of the xanthine series may be used with equal effect) (8) administration of sedatives preferably the barbiturates (9) prevention of abdominal distention by careful regulation of the bowels and food intake (10) reduction regimen for obese patients (11) careful evaluation of the patient s daily activities in order to outline a routine to reduce heart strain to a minimum

*Surgical Treatment of Heart Failure* —Various surgical procedures have been suggested for the treatment of congestive heart failure Essentially these are attempts to relieve the strain on the heart

Valvulotomies and valvuloplasties as well as commissurotomies have been performed in the presence of mitral stenosis These operations involve considerable risk but

some of them offer a certain degree of hope An operation to diminish the strain on the left auricle consists in anastomosing one branch of the pulmonary vein to the azygous vein This results in a short circuiting of some of the blood from the left auricle to the systemic venous circulation It results in effect in a recirculation of blood, but though it may partially reduce the strain on the left auricle it is doubtful whether this is the final answer to the problem

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STARR I and SCHROEDER H A Ballistocardiogram Normal Standards Abnormalities Commonly Found in Diseases of the Heart and Circulation and Their Significance J Clin Invest 1940 *19* 437

*Congenital Heart Disease*

BING R J The Physiology of Congenital Heart Disease Chapter VI Nelson s Loose Leaf Medicine, 1949

BING R J VANDAM L D and GRAY F D Physiological Studies in Congenital Heart Disease II Results of Preoperative Studies in Patients with Tetralogy of Fallot, Bull Johns Hopkins Hosp 1947 *80* 121

BRISWOLD H E BING R J HANDELSMAN J C CAMPBELL, J A and LEBRUN E Physiological Studies in Congenital Heart Di ease VII Pulmonary Arterial Hypertension in Congenital Heart Disease Bull Johns Hopkins Hosp 1949 *83* 76

CAMPBELL J A BING R J HANDELSMAN J C and GRISWOLD H E Physiological Studies in Congenital Heart Disease VIII The Physiological Findings in Two Patients with Complete Transposition of the Great Vessels Bull Johns Hopkins Hosp 1949 *84* 269

DEXTER L HAYNES F W BURWELL C S EPPINGER E C, SAGERSON R P and EVANS J M Studies of Congenital Heart Disease J Clin Investigation 1947 *26* 554

DOW J W LEVINE H D, ELKIN M HAYNES F W HILLERNS H K WHITTENBERGER J W FERRIS B G GOODALE W T HARVEY W P EPPINGER E C and DEXTER L Studies of Congenital Heart Disease Circulation 1950 *1* 267

TAUSSIG H B Congenital Malformations of the Heart New York The Commonwealth Fund 1947

WOOD P Congenital Heart Disease, Brit Med J Sept 16 and 23 p 639 and 693 1950

*Clinical Disorders of the Heart Beat*

BELLET S Clinical Disorders of the Heart Beat Med Clinics N A 1946 *5* 190

DIPALMA J R and SCHULTZ J E Antifibrillatory Drugs Medicine 1950 *29* 123

GOLDMAN I R BLOUNT S G JR FRIEDLICH A L and BING R J Electrocardiographic Observations During Cardiac Catheterizations Bull Johns Hopkins Hosp 1950 *86* 141

LEWIS SIR THOMAS The Mechanism and Graphic Registration of the Heart Beat London Shaw and Sons Ltd 1925

LINENTHAL A J and FREEDBERG A S Measures Used in the Prevention and Treatment of Cardiac Arrhythmias New Eng J Med 1949 *241* 570 and 612

PRINZMETAL M BRILL I C CORDAY E SELLERS A L FLIEG W A and KRUGER H E The Nature of Auricular Flutter J Clin Investigation 1949 *28* 804

*Heart Failure*

BATTERMAN R C and DEGRAFF, A C Comparative Study on the Use of the Purified Digitalis Glycosides Digoxin Digitoxin and Lanatoside C for the Management of Ambulatory Patients with Congestive Heart Failure Am Heart J, 1947 *34* 663

BURWELL W B and HENDRIX J P Digitalis Poisoning Am J Med 1950 *8* 480

ELLIS L B Mechanism of Heart Failure and Related States New England J Med 1943 *228* 284 and 311

FISHBERG A M Heart Failure, 2nd ed Philadelphia Lea & Febiger 1940

GOLD H CATTELL M, MODELL W KWIT N T KRAMER M L and ZAHM W Clinical Studies on Digitoxin (Digitaline Nativelle) with Further Observations on Its Use in the Single Average Full Dose Method of Digitalization J Pharmacol and Exper Therap 1944 *82* 187

*HARRISON T R Failure of the Circulation* Baltimore The Williams & Wilkins Co 1939

PITTS R F and SARTORIUS O W Mechanism of Action and Therapeutic Use of Diuretics J *Pharmacol and Exper Therapeutics 1950 98* 161

SCHEMM F R High Fluid Intake in Management of Edema Especially Cardiac Edema Details and *Basis of* Regime Ann Int *Med 1942* *17*, 952

WARREN J V and STEAD E A JR Fluid Dynamics in Chronic Congestive Heart Failure *Interpretation of Mechanisms Producing Edema* Increased Plasma Volume and Elevated Venous Pressure in Certain Patients with Prolonged Congestive Failure Arch Int Med 1944 *73* 138

*Surgery of the Heart and Great Vessels*

BECK C S STANTON E BATINCHOCK, W and LEITER E Revascularization of the Heart by Grafting a Systemic Artery or a New Branch from the Aorta into the Coronary Sinus J A M A 1948 *137* 436

BLALOCK A and TAUSSIG H B Surgical Treatment of Malformations of Heart in Which There is *Pulmonary Stenosis* or *Pulmonary* Atresia J A M A 1945 *128* 189

CARTER B N Surgery of the Heart and Allied Great Vessels J A M A 1948 *138* 1207

*CRAFOORD C and NYLIN G Congenital Co*arctation of Aorta and Its Surgical Treatment J Thoracic Surg 1945 *14* 347

GLOVER R P O NEILL T J E and BAILEY C P Commissurotomy for Mitral *Stenosis* Circulation 1950 *1* 329

GROSS R E Surgical Relief for Tracheal Obstruction from Vascular Ring New England J Med 1945 *233* 586

POTTS W J SMITH S and GIBSON S Anastomosis of Aorta to Pulmonary Artery Certain Types in Congenital Heart Disease J A M A 1946 *132* 627

THOMPSON S A RAISBECK M J The Surgical Rehabilitation of the Coronary Cripple Ann Int Med 1949 *31* 1010

*Syncope of Cardiovascular Origin*
*(Carotid Sinus Syndrome)*

DRAPER A J The Cardioinhibitory Carotid Sinus Syndrome Ann Int Med 1950 *32* 700

ENGEL G L Mechanisms of Fainting J Mt Sinai Hosp 1945 *12* 170

——— Fainting Physiological and Psychological Considerations Springfield Illinois Charles C Thomas October 1950

NATHANSON M H Hyperactive Cardioinhibitory Carotid Sinus Reflex Arch Int Med 1946 *77* 491

WEISS S and BAKER J P The Carotid Sinus Reflex in Health and Disease Medicine 1933 *12* 297

*Bacterial Endocarditis Acute and Subacute*

BLOOMFIELD A L The Present Status of Treatment of Subacute Bacterial Endocarditis Circulation 1950 *2* 801

GORLIN R FAVOUR C B and EMERY F J Long Term Follow up Study of Penicillin Treated Subacute Bacterial Endocarditis New Eng J Med 1950 *242* 995

LITTMAN D and SCHAAF R S Therapeutic Experiences with Subacute Bacterial Endocarditis New England J Med 1950 *243* 248

ORGAIN E S and DONEGAN C K The Treatment of Bacterial Endocarditis Ann Int Med 1950 *32* 1099

*Myocarditis*

FINE I BRAINERD H and SOKOLOW M Myocarditis in Acute Infectious Diseases A Clinical and Electrocardiographic Study Circulation 1950 *2* 859

FRENCH A J and WELLER C Interstitial Myocarditis Following the Clinical and Experimental Use of Sulfonamide Drugs Am J Path 1942 *18* 109

GORE I and SAPHIR O Myocarditis A Classification of 1402 Cases Am Heart J 1947 *34* 827

SAPHIR O Isolated Myocarditis Am Heart J 1942 *24* 167

*Arteriosclerotic Cardiovascular Disease*

BILLINGS F T JR KALSTONE B M SPENCER J L BALL C O T and MENEELY G R Prognosis of Acute Myocardial Infarction Am J Med 1949 *7* 356

DOSCHER N and POINDEXTER C A Myocardial Infarction without Anticoagulant Therapy Am J Med 1950 *8* 623

EPSTEIN F H and RELMAN A S Transfusion Treatment of Shock Due to Myocardial Infarction New Eng J Med, 1949 *241* 889

GILBERT N C FENN G K and NALEFSKI L A Rôle of Vasodilator Drugs in Coronary Occlusion J A M A 1949 *141* 892

HILL H N Masked Myocardial Infarction Am J M Sc 1950 *219* 394

WRIGHT I S The Modern Treatment of Coronary Thrombosis with Myocardial Infarction Circulation 1950 *2* 939

WRIGHT I S MARPLE C D and BECK D F Report of the Committee for the Evaluation of Anticoagulants in the Treatment of Coronary Thrombosis with Myocardial Infarction Am Heart J 1948 *36* 301

*Cardiovascular Syphilis*

CLAWSON B J Syphilitic Cardiac Deaths in Over 50 000 Autopsies Minn Med 1950 *33* 437

EDEIKEN J FORD W T FALK M S and STOKES J H Penicillin Treatment of Patients with Cardiovascular Syphilis in Congestive Failure Circulation 1950 *1* 1355

MOORE J E Cardiovascular Syphilis Am J Syph 1949 *33* 43

*Cor Pulmonale*

BAKER D V JR WARREN R HOMANS J and LITTMAN D Pulmonary Embolism New Eng J Med 1950 *242* 923

CARROLL, D Chronic Obstruction of Major Pulmonary Arteries Am J Med 1950 *9* 175

McGINN S and WHITE P D Acute Cor Pulmonale Resulting from Pulmonary Embolism Its Clinical Recognition J A M A 1935 *104* 1473

SPAIN D M and HANDLER B J Chronic Cor Pulmonale Arch Int Med 1946 *77* 1

# THE HEART IN SPECIAL CONDITIONS

## HEART DISEASE AND PREGNANCY

BY GEORGE DAVID GECKELER M D
and WILLIAM LIKOFF M D

THE importance of heart disease in pregnancy is reflected in the fact that it is estimated that 2 per cent of all prenatal patients have some form of cardiac disorder The mortality in that group is five times as great as in patients with normal hearts Viewed from a different statistical standpoint heart disease accounts for 25 per cent of all maternal deaths

Whether it is safe for a woman with a cardiac ailment to bear children may be a difficult decision to make. To appraise the problem, the physician must have full knowledge of the nature and severity of the heart lesion. He must understand the essential changes which occur in the circulation during pregnancy, how they may simulate organic heart disease, and the manner in which they may compromise the function of an impaired cardiovascular system.

That is by no means the full task. To conclude the problem successfully, he must be prepared to supervise the patient constantly, seeking out the signs and symptoms of impending trouble. When these are discovered, he must be prepared to treat them with definitive measures.

Only with knowledge, skill, and seasoned judgment are the problems presented by diseases of the heart and pregnancy adequately defined and met. The final estimate of success is in the reduction of maternal and fetal mortality.

*The Circulation in Pregnancy*.—The most significant change in the circulation during pregnancy is the increase in cardiac output. This amounts to approximately 50 per cent in minute volume at the time the output is at its greatest magnitude.

It was formerly believed that the burden on the circulation increased steadily and reached its peak at term, but it has now been demonstrated that the increase in cardiac output is not great before the twelfth week. From that point it rises gradually until the 24th week, and then more abruptly until the 32nd or 36th week, when it lessens to half its rise. Although exactly when the reducing of the burden takes place is not identically fixed by all investigators, there is complete agreement on the cyclic increase and decrease is output *before* term.

Associated with these changes are parallel alterations in blood volume and circulation rate. The average increase in blood volume is 45 per cent and is accounted for by an increase in the plasma volume. The progressive dilution of blood reaches its peak approximately in the 32nd week, after which it gradually returns to more normal values. A corresponding fluid retention takes place in the tissues. Since a positive salt balance has been demonstrated during gestation and a negative balance during the latter weeks of pregnancy and in the puerperium, it is probable that this alteration accounts for the water retention in both the blood and extracellular fluids.

Although a moderate elevation in arterial pressure and cardiac output is observed during labor, the increased burden on the circulation at that time is less than when the output is at its maximum level during pregnancy.

Changes also occur in pulmonary function. The respiratory reserve falls during pregnancy as the result of a 50 per cent increase in pulmonary ventilation. This is accompanied by an increase in respiratory excursions, although actually oxygen consumption is only from 15 per cent to 20 per cent greater than normal. Because of an increase in the transverse diameter of the chest, which overcompensates for the elevation of the diaphragm, a slight increase in the vital capacity of the lungs is observed.

The critical fact in these physiologic alterations in the circulation during pregnancy is that the increase in burden reaches its peak *before* term and is dependent upon rises in cardiac output and blood volume. The mechanism for the increase in blood volume is not fully understood, but the retention of salt and water is an important factor. *The clinical manifestations found in pregnant cardiacs stem from those changes which are common to all child-bearing patients.*

*Types of Heart Disease Found in Pregnancy*.—The types of heart disease seen in pregnancy are those observed in any group of young adults. More than 90 per cent are the result of rheumatic activity. Mitral stenosis is the most common lesion and in combination with aortic disease is more usual than aortic involvement alone or any other combined valvular damage.

In a series of 437 cases Jones found that 6.8 per cent of the patients had congenital heart disease and 2.1 per cent hypertensive cardiovascular disease. These figures approximate those of Hamilton. Cardiac disorders caused by arteriosclerosis, syphilis and thyrotoxicosis are not commonly met

(they make up on the average only one per cent of the total)

In view of the tremendous strides made by cardiac surgery in recent years the opportunity will shortly be offered of supervising young women who have had congenital heart defects corrected by surgery and who have for example, undergone such a procedure as mitral commissurotomy Experience is also increasing with patients who have become pregnant after recovering from subacute bacterial endocarditis

*The Diagnosis of Heart Disease in Pregnancy* —Certain cardiovascular signs and symptoms develop with any ordinary gestation They are similar to those observed in any patient with a hyperkinetic heart and must be differentiated from the more specific clinical features of organic cardiac disease

*Palpitation* is an extremely common complaint It occurs independent of activity and is very often caused by numerous premature systoles which originate in the atrium or ventricle Atrial fibrillation is an exceptionally uncommon arrhythmia in normal pregnancy and its presence almost always indicates serious heart disease

*Dyspnea* is reported by more than half of all normal pregnant women It is actually the result of the increased pulmonary ventilation which occurs even at rest This is never accompanied by fine basal rales cough the production of frothy sputum or a fall in vital capacity

*Tachycardia* is not marked in normal pregnancies although the patient may be conscious of the acceleration of the pulse rate which averages from ten to twenty beats a minute Generally the hyperkinetic action of the heart is misinterpreted by the patient as a tachycardia

*Edema* of the lower extremities is usual in 50 per cent of all normal pregnancies It is the result of salt and water retention and the compression of the pelvic veins by the enlarged uterus

*Pain* over the precordial area is an unexplained symptom It is usually sharp and of short duration and occurs mainly at rest It may well disappear when the patient is gainfully occupied

The *apical impulse* of the heart may be dislocated upward and outward and, because of its position simulate cardiac enlargement Inasmuch as this finding is rarely the sole basis for a diagnosis of heart enlargement serious confusion rarely results

The *first heart sound* is loud at the apex in normal pregnancies The intensity may be similar to that heard in thyrotoxicosis At the second left interspace, the second heart sound is also usually accentuated

*Murmurs* are heard in more than 50 per cent of all normal women who are pregnant The murmurs are usually blowing systolic murmurs generally grade one or two and may be heard at the apex or more often at the base of the heart It must be emphasized that such normal murmurs are blowing highly localized and systolic They frequently disappear with a change in the depth of respiratory excursions or with alterations in body position and posture

A *third heart sound* may be heard in normal pregnancies It may occur in any adult with hyperkinetic heart action Its importance depends on whether it can be differentiated from a gallop rhythm with a rapid heart rate and from the opening snap of mitral stenosis

The *roentgen examination* of the normal heart in pregnancy may at times give rise to some confusion The postero-anterior view may reveal an apparent straightening of the left border, a condition mimicking the silhouette of mitral stenosis Furthermore in the right anterior oblique position the left atrium may appear enlarged These findings are satisfactorily eliminated by x raying the patient at the height of inspiration Although the cardio-thoracic ratio is not entirely reliable under any circumstances it may be greater than the 50 per cent critical value in normal pregnancies since the transverse diameter of the heart is increased by the elevation of the diaphragm

The *electrocardiogram* may reveal a shift in the electrical axis to the left and a negative $T_3$ accompanied by a deep $Q_3$ This is the result of the horizontal position of the heart and is not commonly confused with the changes observed in coronary-artery disease

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materially impaired This is not the general feeling Along with Hamilton, Maynard believes that atrial fibrillation has the same ominous meaning as congestive heart failure and that it increases the risk of death in pregnancy fourfold

4 *The Degree of Cardiac Enlargement* — In no sense is the extent of cardiac enlargement alone an accurate guide to the severity of heart disease Similarly the absence of enlargement is not an indication that a patient will successfully pass through pregnancy

5 *The Presence of Active Rheumatic Infection* —Active rheumatic fever is most uncommon in pregnant patients When it does occur however, particularly in the first trimester a termination of the pregnancy is advisable If the pregnancy is far advanced continuation is safer than interruption

6 *The Presence of Subacute Bacterial Endocarditis* —With the introduction of antibiotics subacute bacterial endocarditis discovered during pregnancy can be successfully treated The death rate may be somewhat higher for pregnant women with subacute bacterial endocarditis, but there is no evidence that a patient who has been cured of the disease successfully will develop a recurrence of it during later pregnancies

7 *Hypertension* —An elevation in the arterial blood pressure is not a serious complication of pregnancy in patients who have cardiac heart disease It does however increase the hazard of toxemia Furthermore, there is evidence that the hypertension in itself may be accelerated by the pregnancy

8 *The History of Prior Heart Failure* — A history of congestive heart failure makes future pregnancy as risky as does the presence of heart failure This is particularly true if acute pulmonary edema has occurred

9 *Hemoptysis* —This is usually the result of pulmonary infarction or pulmonary hypertension In either case it is a contraindication to pregnancy Only in the rare instance when hemoptysis occurs following peripheral venous thrombosis that has been adequately treated is pregnancy to be considered

10 *Parity* —There is little evidence to suggest that parity has any influence on the prognosis of a pregnancy provided the patient s condition has not materially altered between pregnancies It should be emphasized, however, that the care of a child is more difficult for the older woman particularly when previous offspring demand their allotment of time and energy When a family is complete and the maternal health has been safeguarded through several pregnancies, it seems unwise to encourage further childbearing that will demand a greater expenditure of cardiac reserve at an age when it can be least spared

In patients with congenital heart disease the acyanotic tolerate pregnancy well It appears that the greater the degree of cyanosis the more uncertain the prognosis Coarctation of the aorta affords particular concern in the acyanotic group because of the risk of rupture of the aorta acute left ventricular failure and cerebral hemorrhage These are more likely to occur during labor than during gestation

If cardiac function is adequate pregnancy is not clearly harmful to patients with hypertensive and arteriosclerotic heart disease There is adequate evidence however that hypertension may be accelerated by pregnancy Patients with severe hypertension and azotemia are considered poor risks and in the same category as those with congestive heart failure resulting from rheumatic heart disease Although coronary heart disease is extremely rare in pregnant women, it is a firm contraindication to pregnancy

Of the infrequent cases of syphilitic heart disease complicated by pregnancy aortic regurgitation is most common This is recognized as a severe complication Cases however have been reported in which pregnancy was successfully completed in the presence of marked aortic regurgitation In this lesion as in others all influencing factors and the state of compensation must be evaluated before pregnancy is permitted

*The Management of the Pregnant Cardiac Patient* —The patient with heart disease should be advised as early as possible whether future pregnancy is advisable Under those circumstances when pregnancy

With a clear knowledge of the cardiovascular signs and symptoms in ordinary pregnancies, the diagnosis of organic heart disease is greatly simplified

In every instance, an accurate diagnosis should be made in conformity with the standards of the American Heart Association

The *history* is only a partial guide to the presence of rheumatic heart disease, inasmuch as 50 per cent of the patients with rheumatic heart disease have no knowledge of having had an attack of rheumatic fever When the history is positive it aids in classifying the patient in relation to the natural progress of the disease Thus, the number of attacks of rheumatic fever, their severity, and the time of their occurrence in relation to the pregnancy are critical bits of information It is important that congestive heart failure paroxysmal tachycardia embolic phenomenon, subacute bacterial endocarditis and hemoptysis be searched for in the history Finally in view of the impending increased burden upon the circulation, it is essential to investigate how competently the patient has been able to withstand the rigors of ordinary living

Since the patient is in the younger age group and subjective symptoms of cardiac embarrassment may not yet be present a proper diagnosis may rest solely upon the objective examination *The discovery of a valvular lesion may be the only evidence of rheumatic heart disease*

In many cases of mitral stenosis the mid late diastolic murmur with or without presystolic accentuation may not be heard when the patient is at rest This emphasizes the importance of examining the patient after brief but vigorous exercise Even after exercise the murmur may be highly localized and heard only in the left lateral position when the breast is held to one side

Other important auscultatory features may be heard in mitral stenosis The first heart sound may be sharp *i e*, short and high pitched this is to be differentiated from the loud first heart sound of normal pregnancies When it is accompanied by an accentuated pulmonic second sound the physician should be particularly alert in his search for a mid late diastolic murmur On the other hand, the opening snap of a mitral stenosis may be heard This must be differentiated from a normal third heart sound Although the opening snap does not necessarily bear a closer time relation to the second heart sound, it is of uniformly greater intensity than the normal third sound and is usually accompanied by an accentuated pulmonic second sound and a mitral systolic murmur The differentiation between the opening snap of mitral stenosis and gallop rhythm with tachycardia may be extremely difficult, other features, however may help the physician to make it

The murmurs of congenital heart lesions may be so impressive that they can not be overlooked in the most casual physical examination Often, however major defects such as the tetralogy of Fallot or large septal defects, exist without loud murmurs In such cases, investigation for cyanosis and clubbing of the fingers is of great importance

The cardiac examination during pregnancy should include (1) a roentgen survey for heart size and contour and (2) an electrocardiogram These procedures occasionally point to heart disease that is not readily apparent

*Significant Factors in the Pregnant Cardiac* —The greatest cause of death when pregnancy accompanies structural heart disease is heart failure, and the most common type is pulmonary edema Embolic phenomenon and subacute bacterial endocarditis are much less frequently fatal Therefore the most important factor which makes for a successful pregnancy is the state of cardiac compensation

1 *Age* —Rheumatic cardiacs are more likely to develop congestive heart failure in pregnancy as they become older

2 *Duration of Heart Disease* —As the interval of time lengthens from the onset of rheumatic fever to pregnancy the incidence of such failure rises

3 *The Presence of Atrial Fibrillation* —This arrhythmia implies that the heart disease is both long standing and severe In its presence the risk of pregnancy is grave Jones believes however that the arrhythmia itself is not a complication of pregnancy and suggests that pregnancy may be allowed if the capacity for effort is not

cardiovascular apparatus may fail with time The economic status of the patient the completeness of the family the personality of the mother and the manner in which she reacts to children are all factors entering into the problem

*Patients Unfit for Pregnancy* —When a cardiac patient who is unfit for pregnancy is seen in the first trimester interruption of pregnancy should be advised This termination should not take place in the face of acute congestive heart failure or other serious illness Under all circumstances the heart must be compensated before abortion is attempted

In the second trimester, an interruption of pregnancy is rarely indicated When heart failure is present in the early part of the second trimester and the response to therapy has not been adequate interruption of the pregnancy may be advisable since the patient is still faced with months of a progressive burden on the circulation This problem is an extremely difficult one and entails grave risk

In the third trimester interruption of the pregnancy is rarely indicated the load on the circulation will decrease with time and medical control is more likely to succeed

In any or all circumstances the mode of termination is a problem for the obstetrician

*Treatment of Heart Failure* —The treatment of heart failure in the pregnant patient is along the usual lines When acute pulmonary edema is present (in view of the fact that it is due at least in part to an increase in blood volume), rapid venesection may be indicated The use of morphine and oxygen and intravenous digitalis preparations is fundamental and may clear up an ominous clinical state

Chronic congestive heart failure is best treated by gradually increasing rest as the load on the circulation increases This rest is preferable in the semi recumbent position in order to shift fluid concentrations to the extremities A diet low in salt (1 2 Gm of salt a day) is strongly recommended Once digitalis is used it should be continued throughout the pregnancy Although there is some danger in using the mercurial diuretics in pregnancy in which there is always the possibility of renal damage the drugs are not to be withheld when indicated Finally the salt absorbing resins may greatly aid in keeping the patient upon a salt poor routine

*Confinement* —The mode of delivery is subject to the judgment of the obstetrician Hamilton and Thomson have shown that, among cardiac women the mortality in vaginal delivery is 2 3 per cent as compared to 8 3 per cent for abdominal deliveries

With coarctation of the aorta a catastrophic accident may occur during labor and abdominal delivery may be advisable particularly when the patient is over thirty years of age

A trial of labor is rarely indicated in the presence of heart disease The manner of delivery should be decided upon well in advance and the patient properly prepared in order to avoid the hazards which accompany indecision

*Post Partum Care and Future Pregnancies* —Convalescence from pregnancy is determined by the severity of the cardiac lesion As a general rule, when the cardiac condition is marked the convalescence should be prolonged The state of compensation determines the degree of activity A woman who has once been in congestive heart failure is never a candidate for future pregnancy

REFERENCES

ANTHONY A J and HANSON R Lungenventilation und Atmung in der Schwangerschaft (1935) Ztsch L Geburtsch u Gynak 1935 *105* 138
APPEL T W Congestive Heart Failure in Pregnancy Amer J Obs Gyn 1940 *39* 24
BUNIM J J and APPEL S B J A M A 1950 *142* 90
BUNIM J J and RUBRICIUS J The Am Heart J 1948 *35* 282
BUNIM J J and TAUBE H Med Clin N Amer 1951 May 674
CHESLEY L C Amer J Obs and Gyn 1944 *48* 565
COHEN M E and THOMSON K J New Eng J Med 1936 *214* 905
——— J Clin Invest 1936 *15* 607
HAMILTON BURTON E Am Heart J 1947 *33* 663
HAMILTON B E and THOMSON K J The Heart in Pregnancy and the Childbearing Age Little Brown & Co Boston 1942
HAMILTON H F H J Obs Gyn Brit Emp 1949 *56* 548
JONES A MORGAN Heart Disease in Pregnancy Grune & Stratton Inc New York 1951
MAYNARD E P JR Medical Clinics of N Amer 1950 May 795

is possible but not desired, the patient should be instructed to have her physical condition thoroughly reviewed before pregnancy is contemplated When pregnancy occurs before re evaluation has been made, the patient should be re-examined as soon as possible

In women with heart disease fitness for pregnancy can best be determined by an analysis which enables one to place the patient in a functional classification as suggested by the American Heart Association Patients who have no limitation of activity (Class I) rarely if ever, have a serious complication in pregnancy In the series recorded by Pardee no deaths occurred among 157 pregnant women with this functional capacity Patients who have slight or moderate limitation of activity (Class II) seldom develop serious complications either But patients who have from moderate to great limitation of activity (Class III) frequently fail to survive pregnancy and patients unable to carry on any physical activity without embarrassment (Class IV) commonly die in pregnancy

This functional classification should be augmented by an analysis of other factors which materially affect the outcome of the pregnancy

*Patients Fit for Pregnancy* —The basis of the management of heart disease during pregnancy is the prevention of heart failure If this is not possible emphasis must be placed on early diagnosis of the failing heart and on efficient treatment Most pregnant women with heart disease will do well provided careful examinations are carried out every month for the first seven months every two weeks during the eighth month and every week during the ninth month In these examinations particular attention must be paid to the features of incipient heart failure, namely dyspnea, cough bilateral pulmonary rales hepatomegaly unusual edema, and tachycardia Great care must be exercised in the prevention of respiratory infections These may readily precipitate cardiac failure Infections such as the common cold and sore throat must be treated as major events

It is well to prevent unusual and explosive effort on the patient s part particularly in those months of pregnancy when the circulatory burden is greatest Most pregnant cardiacs should have a minimum of ten hours rest at night and two hours rest in mid afternoon Invalidism, however, is not to be encouraged and reasonable muscular activity is beneficial

Excessive weight may be prevented by diets low in calories and a reasonable sodium restriction If the sodium intake is reduced to only 2 Gm a day, weight loss will follow and the tendency to fluid retention will be lessened

Inasmuch as anemia increases heart output, it is to be actively treated with iron and folic acid Because of the degree of hemodilution a complete correction of anemia is unusual (*See* Chapter 25)

Subacute bacterial endocarditis may develop in one per cent of the pregnant patients with rheumatic heart disease As a precaution dental sepsis should be treated promptly with antibiotics, extensive dental repair should be avoided during pregnancy (unless absolutely necessary)

*The Management of Confinement* —The management of confinement is principally a matter for the obstetrician In all good risk patients labor should be allowed to pursue its normal course The second stage of labor may be shortened by a low forceps delivery It is advisable to give penicillin as a prophylactic agent when labor begins

*The Management of the Post Partum Period* —If the patient is not too exhausted by the procedure nursing is permissible and encouraged Since the circulatory changes in pregnancy regress slowly perhaps over a period of from three to six weeks, activities during this time should be as well guarded as they are during the months of pregnancy

*Future Pregnancies* —It is advisable for the cardiac patient to discuss future pregnancies with the physician at an early date Following delivery a full return to the normal physiologic state may take as long as a year or a year and a half If the cardiac status has not deteriorated a second pregnancy should not be ventured before that time has passed At the same time long intervals between pregnancies are inadvisable because the integrity of the

relationship to arterial supply differentiate these lesions from true infarctions of the heart muscle secondary to coronary artery insufficiency In most instances the myocardial bruising by trauma heals without trace However, nonfatal massive necrosis in the wall of the left ventricle following trauma has occasionally led to formation of aneurysm of that chamber

In the experimental animal cardiac traumatism has caused various types of heart block, presumably due to hemorrhagic infiltration of conduction bundle tissue This has seldom been seen in human hearts but hemorrhagic infiltration of the walls of the auricles a condition productive of arrhythmia is common especially in areas of junction with the great vessels Thus hemorrhage around the orifice of the inferior vena cava and spreading into the adjacent auricular structure is frequently noted after crush injury of the lower chest at or near the mid line Another interesting junctional lesion but one without effect on cardiac rhythm is laceration and rupture in the root of the aorta A traumatic dissecting aneurysm of the aorta just above the valve leaflets will occasionally be seen by every coroner s physician

Valvular damage subsequent to nonpenetrating chest trauma is rare Traumatic rupture of an aortic leaflet has apparently occurred in normal hearts such occurrence appears more plausible in leaflets thickened by syphilis Mitral insufficiency following rupture of the chordae tendinae and papillary muscles subsequent to cardiac traumatism has also been reported The incidence of infectious endocarditis, however, mostly of the acute ulcerative type, but also occasionally of the subacute bacterial type following traumatism in distant portions of the body (which presumably has caused local cellulitis and then sepsis), is greater The involved leaflets are generally the site of previous pathology

*Clinical Aspects* —In cardiac traumatism following direct penetrating chest injury, the heart action is rapid the heart sounds are feeble there is occasionally the friction or splash of hemopericardium Frequently the signs of cardiac tamponade are present this if opportunity permits may be verified by fluoroscopy If a coronary artery has been lacerated, electrocardiographic changes may quickly appear They may be due to pericardial reaction to hemopericardium Some or all of these signs may be noted in any case depending on the extent of the traumatism the degree of emergency and the opportunity for examination Where death has not quickly supervened penetrating or lacerating cardiac trauma most commonly results in tamponade in which diastolic filling of the ventricles is hampered by hemopericardium This is evidenced by a small rapid pulse low blood pressure small pulse pressure increasing venous pressure cyanosis and acute congestion of the liver Shock a common accompaniment may add to or confuse the clinical picture

Cardiac trauma following nonpenetrating chest injury presents a marked variation in its clinical aspects, depending on the site of the injury on the chest wall the manner and degree of the applied force the absence or presence of thoracic bone fracture the extent of the accompanying pleural and pulmonary damage and the age and previous health of the patient In patients rendered unconscious by the accident physical signs afford the only clue Rapid feeble heart action especially in the presence of chest injury, is a common sign of cardiac trauma Rapid arrhythmia is striking confirmation in many cases Repeated electrocardiographic examinations show evidence of abnormality and shifting functional status The conscious patient often speaks of pain at the time of the accident or a few hours later It ranges from a dull nonradiating precordial discomfort to typical angina pectoris Palpitation is commonly mentioned Blood spitting and pain on deep breathing indicate at least intrathoracic traumatism and though generally of pleural and pulmonary origin may have a cardiac significance Cyanosis may or may not be present Congestive heart failure with hepatomegaly and leg edema seldom makes an early appearance unless the heart has been previously involved in advanced spontaneous disease

The time factor is important in the clinical picture of nonpenetrating cardiac trauma-

MENDOLSOHN C I Amer J Obs Gyn 1944 *48* 329
PARDEE H E B J A M A 1934 *103* 1889
REID, D E and TEEL H M J A M A 1939 *113* 1628
STANDER H J and KUDER K J Amer Med Assn 1937 *108* 2092
THOMSON K J HIRSHEIMER A and GIBSON J G Amer J Obs Gyn 1938 *36* 48
THOMSON K J and COHEN M E Surg Gyn Obs 1938 *66* 501

## CARDIAC TRAUMA

BY BENJAMIN A GOULEY, M D
and WILLIAM G LEAMAN, M D

Cardiac trauma is not so uncommon as previously believed As a result of high speed transportation and industrialization, it has become an important medico legal and clinical entity

*Definition* —This chapter deals with cardiac trauma characterized by structural damage within the heart, in the pericardium, and at the junctional areas of entrance and emergence of the great vessels Profound and fatal physiological disturbance of cardiac function following traumatism in other portions of the body is not included

*Etiology* —Cardiac injury may follow a penetrating wound of the chest wall or a blunt injury, the so-called nonpenetrating chest traumatism Occasionally, sudden compressive injury of the abdomen or a fall from a height may produce intracardiac laceration, especially in the thin walls of the atria Penetrating wounds of the heart result most often from a stab with a knife or other sharp pointed weapon Gunshot wound is a common cause of cardiac injury Flying glass or the like as during a bombing may also penetrate the chest and damage the heart And puncture of the heart by broken ribs is sometimes seen in automobile and airplane accidents Compression of the heart following the application of force to the chest in the antero posterior diameter accounts for most nonpenetrating cardiac traumatism

*Pathology* —The right ventricle is the most common site of direct penetrating injury since the greater part of this chamber is presented anteriorly However the right atrium and the left ventricle are also vulnerable, and the coronary arteries and veins may be lacerated, with resulting hemopericardium and tamponade Since objects producing direct injuries are usually contaminated purulent pericarditis is a common complication, generally followed by adhesion

Nonpenetrating injuries may damage the pericardium, the myocardium, or the valves Involvement of the coronary arteries by nonpenetrating injuries of the chest remains a controversial issue Proved cases have not occurred in the experience of the writers except for instances of massive injury, immediately fatal as the result of widespread crush of the heart Some degree of pericardial inflammation is present in every case of cardiac trauma It may remain localized over the site of the application of force, or it may involve a large portion or all of the pericardial surface In contrast to the pericardial reaction to contaminated puncture this type of pericarditis is nonsuppurative it may be hemorrhagic and fibrinous It seldom gives rise to widespread adhesion

The myocardium may be so compressed as to lead to acute rupture of either ventricle or of the right auricle With lesser involvement hemorrhagic softening of the myocardium may develop as a focal lesion at the site of the applied force or as sometimes seen in cases of "steering wheel compression, the opposite ventricular wall may be bruised in contre-coup manner Sometimes though not often, the necrosis traverses the width of the ventricular wall and causes a delayed rupture as long as two weeks after the accident Microscopically, one notes hemorrhagic and edematous infiltration of the myocardium with separation and disorganization of the fibers Sarcolysis of individual fibers and leucocytic infiltration of varied type are seen in cases of severe injury of this kind Abscess does not occur and the typical coagulation necrosis of ischemic infarction seldom if ever, occurs The gross aspect however, of such a lesion sometimes simulates that of myomalacia following coronary thrombosis and this has been noted by various writers The tendency to hemorrhage the vague demarcation and the often peculiar localization without

relationship to arterial supply differentiate these lesions from true infarctions of the heart muscle secondary to coronary artery insufficiency In most instances the myocardial bruising by trauma heals without trace However, nonfatal massive necrosis in the wall of the left ventricle following trauma has occasionally led to formation of aneurysm of that chamber

In the experimental animal cardiac traumatism has caused various types of heart block presumably due to hemorrhagic infiltration of conduction bundle tissue This has seldom been seen in human hearts but hemorrhagic infiltration of the walls of the auricles a condition productive of arrhythmia, is common especially in areas of junction with the great vessels Thus hemorrhage around the orifice of the inferior vena cava and spreading into the adjacent auricular structure is frequently noted after crush injury of the lower chest at or near the mid line Another interesting junctional lesion but one without effect on cardiac rhythm is laceration and rupture in the root of the aorta A traumatic dissecting aneurysm of the aorta just above the valve leaflets will occasionally be seen by every coroner s physician

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*Clinical Aspects* —In cardiac traumatism following direct penetrating chest injury the heart action is rapid the heart sounds are feeble there is occasionally the friction or splash of hemopericardium Frequently the signs of cardiac tamponade are present this if opportunity permits may be verified by fluoroscopy If a coronary artery has been lacerated, electrocardiographic changes may quickly appear They may be due to pericardial reaction to hemopericardium Some or all of these signs may be noted in any case depending on the extent of the traumatism the degree of emergency and the opportunity for examination Where death has not quickly supervened penetrating or lacerating cardiac trauma most commonly results in tamponade in which diastolic filling of the ventricles is hampered by hemopericardium This is evidenced by a small rapid pulse low blood pressure small pulse pressure increasing venous pressure cyanosis and acute congestion of the liver Shock a common accompaniment, may add to or confuse the clinical picture

Cardiac trauma following nonpenetrating chest injury presents a marked variation in its clinical aspects, depending on the site of the injury on the chest wall the manner and degree of the applied force the absence or presence of thoracic bone fracture the extent of the accompanying pleural and pulmonary damage and the age and previous health of the patient In patients rendered unconscious by the accident physical signs afford the only clue Rapid, feeble heart action especially in the presence of chest injury, is a common sign of cardiac trauma Rapid arrhythmia is striking confirmation in many cases Repeated electrocardiographic examinations show evidence of abnormality and shifting functional status The conscious patient often speaks of pain at the time of the accident or a few hours later It ranges from a dull nonradiating precordial discomfort to typical angina pectoris Palpitation is commonly mentioned Blood spitting and pain on deep breathing indicate at least intrathoracic traumatism and though generally of pleural and pulmonary origin may have a cardiac significance Cyanosis may or may not be present Congestive heart failure with hepatomegaly and leg edema seldom makes an early appearance unless the heart has been previously involved in advanced spontaneous disease

The time factor is important in the clinical picture of nonpenetrating cardiac trauma-

tism. Though an occasional victim of such injury shows indefinite signs of cardiac embarrassment only to die suddenly two weeks later of a ruptured ventricle, such signs usually foretell gradual, often rapid, clinical improvement. A transient episode of cardiac traumatism is often revealed only by progressive electrocardiographic *change, the symptomatology disappearing* before the tracing returns to normal. Auricular arrhythmia, either fibrillation or flutter, in patients previously free from cardiac disease, may be the most persistent sign of cardiac traumatism. Most instances, however, of such arrhythmia show a spontaneous return to normal rhythm or at least a satisfactory response to therapy.

Arrhythmia, T-wave changes and evidence of pericarditis constitute the major electrocardiographic changes in cardiac trauma. Auricular fibrillation and auricular extra systoles are frequent developments, and they develop quickly after an accident. If they make their appearance some days afterwards, their connection with cardiac traumatism is doubtful. Heart block receives disproportionate attention in the literature. Its occurrence is extremely rare. Typical infarction patterns are seen in the steering wheel compression cases, in which T-2 and T-3 inversion is a common finding and clearly indicative of massive bruising or necrosis of the left ventricular myocardium posteriorly. Contrariwise a typical pattern of anterior apical infarction is seldom seen; indeed a flattening or moderate inversion of T waves in the direct and unipolar leads is the usual electrocardiographic evidence of anterior traumatization in the left and right ventricles. Where S-T elevation develops in many or all leads a traumatic pericarditis is usually present.

The clinical incidence of traumatic pericarditis in the nonpenetrating type of cardiac trauma is much lower than pathologic findings would indicate. A pericardial friction is described in a few of the case reports, but it should be noted that physical examination is often carried out under difficult circumstances. Massive bloody effusions may follow serious compressive injury. They seldom develop after moderate bruising of the myocardium. As previously noted cardiac tamponade is common in the penetrating type of cardiac injury. Suppurative pericarditis—and, occasionally, a residual chronic, constrictive pericarditis—may follow the tamponade. The clinical signs of the small immobilized heart may thus develop following traumatism. But, in most cases of post-traumatic pericarditis the pericardial lesion gradually resolves itself, partially or completely, the patient thus escaping the dreaded complication of constrictive cardiac failure.

*Diagnosis.*—A direct penetrating injury to the heart can be diagnosed promptly on the basis of case history and examination. The physical signs of pericardial friction, of cardiac compression, and of acute cardiorespiratory insufficiency will complete the evidence afforded by the external wound. There are occasions, however, when the external wound is scarcely visible, as for example in puncture wound by ice pick or hat pin. Also, the physical signs may on occasion be indecisive. Pallor and a rapid heart action or a moderate muffling of the heart sounds may be the only changes noted in a patient who dies an hour later as a result of cardiac tamponade. Generally the dramatic aspect of the traumatism and of the physical signs leads to a rapid and accurate diagnosis.

The diagnosis of nonpenetrating traumatism presents numerous difficulties. Where the patient has been the victim of serious thoracic injury as evidenced by external bruising, broken ribs or hemoptysis the possibility of cardiac traumatism should always be considered. In some instances the examiner's attention is drawn to obvious injuries of the head and extremities and the chest is scarcely examined. If in such cases the electrocardiograph were routinely employed the incidence of cardiac trauma would be much greater than current statistics indicate. A tentative diagnosis of cardiac trauma should be made if the electrocardiographic tracing reveals arrhythmia in the absence of previous heart disease. *If the tracing reveals acute pericarditis* the diagnosis is almost certainly that of a traumatic lesion. Thus in people recently injured, in the acute and subacute phase of traumatic reaction the electrocardiogram is of paramount diagnostic importance. Abnormal patterns that show no or only

slight change in serial study are also important as indicating the absence of acute cardiac trauma. Many people who have chronic coronary artery insufficiency are involved in accidents. Tracings which in cases of chest injury show chronic myocardial damage should repeatedly be confirmed at short intervals. A comparison of such tracings will show whether the patient has escaped cardiac injury. Sometimes a pre-traumatic tracing is available for comparison. The limitations of electrocardiography are not to be forgotten in diagnosing and estimating the extent of cardiac trauma. Hemorrhage, shock, acidosis, traumatic pneumonia, pulmonary embolism, anesthesia, digitalis and morphine may cause electrocardiographic signs that cloud the diagnosis or make it impossible. A review of the entire clinical picture is often necessary.

Severe cardiac traumatism by blunt nonpenetrating injury of the chest wall is always accompanied by traumatic pleurisy or pneumonitis or both. Absence of such injury, as shown by clinical and (especially) x-ray examination of the chest, makes the diagnosis of cardiac trauma unlikely. Rare exceptions to this rule probably occur when small objects strike the precordium, as, for example, in golf ball trauma of the heart.

The absence of rib fracture does not exclude cardiac trauma. Children and young adults may suffer cardiac tamponade following nonpenetrating injury without rib fracture. Conversely, in persons over 50 cardiac traumatism of any clinical significance is always accompanied by such injury. The location of the injury is of diagnostic importance. Anterior and anterolateral rib fracture may be accompanied by heart damage, but chest injury leading to lateral rib fracture seldom causes it, and right sided posterior rib fracture is free from such complication. Fracture of the clavicles is not associated with cardiac trauma, but a broken sternum is particularly dangerous and x-ray identification of it lends strong support to the diagnosis of cardiac traumatism.

The diagnosis of cardiac trauma becomes increasingly difficult with the passage of time following an accident. Objective signs disappear and subjective complaints form the basis of many problems in the differential diagnosis. Aside from the rare complications of constrictive pericarditis and aneurysm of the left ventricle, cardiac trauma tends toward complete or satisfactory recovery in people with previously normal hearts. World War II taught us that the problem of the chronic or delayed aspect of cardiac traumatism with respect to both diagnosis and prognosis revolves around the question of the effect of chest trauma on previous cardiac pathology.

The important question of the effect of overexertion on hearts with coronary insufficiency is excluded as not truly relevant. However, the effect of hemorrhage and shock following extra-cardiac trauma on coronary insufficiency is of direct connection. Serious coronary disease is adversely affected, but the evidence must appear within reasonable time limits. If secondary coronary occlusion develops beyond two or at the most three weeks, then connection with a traumatic episode is most unlikely. This conclusion is based on the current knowledge of delayed myocardial infarction following coronary occlusion.

Nonpenetrating nonfatal chest traumatism does not directly injure the coronary arteries, even those involved in previous disease. The histological study of serial sections in many cases of severe chest traumatism, cases representing all age levels, has failed to reveal coronary artery injury even in the presence of myocardial contusion. Rare exceptions may exist in the "steering wheel-compression" cases in which traumatism to the right coronary artery could be obscured by the massive myocardial contusion of the posterior and adjacent septal walls of the left ventricle. Patients, mostly elderly, with advanced coronary artery insufficiency not infrequently die suddenly after trauma or the sight of an accident. Even where the chest has been more or less traumatized, sudden death by coronary insufficiency is best explained by neurogenic, emotional or possibly hormonal factors. Contusion will heal in a myocardium previously scarred by coronary insufficiency, as will infarction, only the scar of the latter is larger.

It is difficult to evaluate the effect of cardiac traumatism on the myocardial disease

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The clinical incidence of traumatic pericarditis in the nonpenetrating type of cardiac trauma is much lower than pathologic findings would indicate A pericardial friction is described in a few of the case reports but it should be noted that physical examination is often carried out under difficult circumstances Massive bloody effusions may follow serious compressive injury They seldom develop after moderate bruising of the myocardium As previously noted cardiac tamponade is common in the penetrating type of cardiac injury Suppurative pericarditis—and, occasionally, a residual, chronic, constrictive pericarditis—may follow the tamponade The clinical signs of the small immobilized heart may thus develop following traumatism But, in most cases of post traumatic pericarditis the pericardial lesion gradually resolves itself partially or completely the patient thus escaping the dreaded complication of constrictive cardiac failure

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cardium Since a primary tumor of the heart may be very small, few if any cardiac symptoms may be present Metastases to adjacent structures, however, may be numerous and are generally the cause of death Even large primary growths in the heart structure may be asymptomatic Signs and symptoms, if present at all depend largely on the anatomical location of the growth For example a pedunculated tumor mass in the left atrium may give rise to signs suggestive of mitral stenosis Again varying degrees of heart block may be the result of invasion of the auriculo ventricular bundle Under these circumstances the Adams-Stokes syndrome may be present and sudden death is not uncommon The appearance of an unexplained pericardial effusion in a patient of any age should alert the clinician to the possibility of a neoplasm Pressure on a coronary vessel by a tumor growth may produce pain of the anginal type Rupture of a sarcoma of the pericardium into the pleural cavity may occur and is generally followed by a rapidly downhill course It is possible for tumors extending into the heart chambers particularly the left atrium to initiate thrombus formation Subsequent embolization may occur Though rare sudden death may follow blocking of the mitral or tricuspid orifices by large embolic masses of tumor cells Congestive heart failure develops in some patients as a result of either invasion of the myocardium or the compression of the heart with hypodiastolic filling which follows extensive pericardial involvement

The roentgen silhouette often reveals the presence of an unexplained irregularity of the cardiac border In some cases if these are investigated a diagnosis of cardiac neoplasm is possible *ante mortem* A ventricular aneurysm however should always be excluded in older patients when a puzzling shadow of this type is encountered

A variety of changes may occur in the electrocardiogram though the tracing is not diagnostic of the lesion Tall P waves accompany atrial involvement and atrial fibrillation is always a possibility Occasionally the picture of acute myocardial infarction may be simulated by an invading tumor T wave changes consistent with that condition may then appear Rarely bundle branch block and heart block occur

Clinical diagnosis of a cardiac tumor is most difficult and is seldom made Better diagnostic results might be obtained if neoplasms were always suspected in connection with bloody pericardial effusion The fluid obtained by paracentesis should always be carefully examined for tumor cells by one trained in the proper procedure If congestive failure of unknown etiology is present and responds poorly or not at all to the usual therapeutic measures the diagnosis of cardiac tumor should always be considered Unexplained heart block belongs in the same category A positive history of neoplasm, either past or present is valuable additional evidence in arriving at the diagnosis In retarded children who present cardiac enlargement with or without murmurs and other congenital defects neoplasm of the heart should be considered

*Treatment* —Benign neoplasms of the heart have been successfully treated surgically The percentage, however is very small it would be higher if the diagnosis were always considered unusual physical findings carefully evaluated, and complete studies made early

The treatment of secondary growths involving the heart is unfortunately, entirely symptomatic If cardiac tamponade develops paracentesis of the pericardium is necessary Deep roentgen ray therapy may be helpful when dealing with a susceptible type of primary lesion Nitrogen mustard and its allies may be tried

*Prognosis* —Complete cure as the result of surgical excision of a primary cardiac tumor is possible, provided the growth is single and benign If metastatic growths are present when the patient first seeks treatment the outlook is hopeless The nature of the growths and their location are always important factors in formulating the prognosis

REFERENCES

Halpern William and Leaman William G Cardiac Compression and Failure Following Metastatic Tumor Infiltration New International Clinics 1939 *4* 213

Yater Wallace M Tumors of the Heart and Pericardium Pathology Symptomatology and Report of Nine Cases Arch Int Med 1931 *48* 627

or the valvular insufficiency of chronic rheumatic heart disease Almost certainly, cardiac trauma does not initiate the rheumatic process it probably does not reactivate it Patients with mitral stenosis have recovered from cardiac stab wounds without congestive heart failure or recurring rheumatic carditis However, patients with subacute myocarditis have not been involved in cardiac trauma in sufficient number to permit conclusive study of the relationship of these factors to each other Syphilitic heart disease, valvular and myocardial has traditionally been considered vulnerable to cardiac trauma It has long been recognized *per se as a cause of sudden death Patients* with luetic aortitis have shown at autopsy, however, no greater incidence of myocardial bruising than nonluetic patients, and certainly those who have survived serious chest traumatism for weeks or months have shown no increased incidence of myocardial gumma

In general, cardiac trauma tends to heal as well in diseased hearts as in normal hearts The process is longer in the former because *of diminished circulatory efficiency associated* metabolic disease or concomitant trauma of the lungs, which may cause more cardiac insufficiency than myocardial bruising itself Intensification by trauma of pre-existing heart disease is more commonly believed to occur than is warranted by the results of pathologic study and objective clinical evidence Thorough examination of the patient and a searching review of his history including his hospital chart following the cardiac traumatism, will often determine whether the trauma existed in the beginning or cardiac neurosis developed later

*Treatment* —If the patient survives a penetrating wound *of the heart until he* reaches the emergency ward surgery is generally necessary Where hemopericardium has been relieved by a single paracentesis operation may be avoided Where the signs of cardiac tamponade continue and are progressive, surgical treatment cannot be delayed Blood transfusion is helpful and often necessary The liberal and immediate use of antibiotic therapy has reduced both mortality and the late complications of suppurative pericarditis and empyema

In the nonpenetrating compressive heart injury, as a result of which cardiac tamponade may develop more insidiously the need for surgical intervention must be constantly *considered In patients in whom* electrocardiographic changes occur following chest traumatism, all activity should be curtailed for two or three weeks, the patient remaining under the same supervision as is given a case of myocardial infarction Quinidine therapy is most appropriate where cardiac irritability is evident The patient may return to his previous activity only when all suspicious signs disappear and the electrocardiogram has become stabilized

## REFERENCES


CUNEWARDENE H O Brit Med J 1934 *2* 1101

HOWARD C P Canad M A J 1928 *19* 12

JOACHIM H and MAYS A T A Case of Cardiac Aneurism Probably of Traumatic Origin Am Heart J 1926 *2* 682

KISSANE R W Contusion of the Heart Ohio State University Columbus Ohio 1937

MORITZ A R The Pathology of Trauma Philadelphia Lea & Febiger 1942


# TUMORS OF THE HEART

By WILLIAM G LEAMAN, M D

Primary or secondary tumor growths of the heart are rare Their cause is unknown Nevertheless, the diagnosis should always be considered in the presence of a heart lesion of unexplained etiology This is particularly true if the patient is of cancer age or has previously had a malignant process in any other part of the body Since the removal of benign or primary cardiac growths is now possible, the outlook for the patient with such a growth is grave but no longer hopeless

*Primary growths of the heart, however,* are less often encountered than metastatic heart growths The benign cardiac tumors include myxoma rhabdomyoma fibroma lipoma and *angioma The malignant* cardiac tumors include round-cell rhabdomyosarcoma epicardial epithelioma, mesothelial sarcoma of the pericardium and other varieties of sarcoma

The left atrium is usually the site of benign growths Primary malignant tumors are more often found in the right atrium the interventricular septum and the peri

and to obtain biopsy material *Bronchography* by utilization of radiopaque material introduced into the bronchus permits a complete survey of the bronchial tree and any existing anomalies, dilatations strictures fistulas, or bronchial occlusions Its use is advocated when there is suspicion of bronchiectasis or of unexplained hemoptysis chronic cough or wheezing exists or chest *x* rays are difficult to interpret It is contraindicated if exudative tuberculosis exists, the patient is debilitated hemoptysis has recently occurred the patient suffers from decreased vital capacity or thyrotoxicosis chronic nephritis or iodine idiosyncrasy exists

Exploratory thoracotomy is a procedure used when other diagnostic measures have been exhausted

*Laboratory Procedures* —(1) One of the most important laboratory procedures in the diagnosis of tuberculosis is examination of sputum Its amount color consistency, odor and content are all of significance Microscopic examination of the sputum may reveal fibers spirals polymorphonuclear leucocytes eosinophiles bronchial casts parasites broncholiths and cancer cells

The sputum is profuse in bronchiectasis and advanced tuberculosis In the former it tends to be three-layered—the top layer frothy white the bottom layer consisting of yellow pus and the middle layer fluid The sputum is frothy and tenacious in asthma rusty in pneumonia pinkish and frothy in passive congestion blood tinged in infarction bronchiectasis and tuberculosis and frankly red in hemorrhage A foul odor is noted in the sputum in bronchiectasis empyema and abscess if bacillus-coli infection is present The sputum in lung gangrene is fetid and contains tissue fragments

The sputum smear may show the presence of the colorless and hexagonal Charcot Leyden crystals of bronchial asthma and bronchitis Dust and metallic particles in the sputum may indicate a pneumoconiosis

(2) Stomach washings may reveal the presence of tubercle bacilli in swallowed sputum Centrifuged specimens smeared on slides for microscopic study or cultured and inoculated into animals have revealed such bacilli in 90 per cent of the cases of tuberculosis with cavitation

(3) The skin tests commonly used are the tuberculin the coccidioidin and the histoplasmin If properly performed these tests are helpful in diagnosis but establish only that infection of the type tested occurred at some previous time and is not necessarily active or even recent With few exceptions a repeated negative reaction rules out the disease in question

(4) Cytologic examination of bronchial washings or sputum may reveal the presence of cancer cells when at least three separate sputa are examined such tests are quite reliable and false positives are few in number Cytologic examination of pleural transudates centrifuged at high speed and the sediment stained with Wright s stain may reveal lymphocytes whereas suppurative exudates show neutrophile leucocytes almost entirely

(5) The erythrocyte-sedimentation test is frequently used as a guide to therapy and prognosis in tuberculosis an accelerated sedimentation rate after prolonged bed rest being a poor prognostic sign Sudden increase in the sedimentation rate may signify impending complications However elevation of the sedimentation rate is not pathognomonic since it is observed in many acute and chronic processes

In diseases of the chest the symptoms are not pathognomonic A symptom seeming to indicate disease of the chest may actually be an expression of involvement of another system of the body while a far advanced lung disease except for possible functional changes may produce no symptoms

*The Clinical Syndrome of Diseases of the Respiratory Tract* —The symptoms most commonly observed in pulmonary disease are cough expectoration dyspnea cyanosis chest pain hemoptysis clubbing of the fingers and toes, fever and polycythemia Any or all of these symptoms may occur in a single case They are helpful to only a small degree in the differential diagnosis of pulmonary infections

*Cough* —Cough is one of the most frequent and most persistent symptoms of pulmonary infections yet it may be slight or entirely

# Chapter 22

# Diseases of the Respiratory Tract

By J WINTHROP PEABODY M D and J WINTHROP PEABODY Jr M D

## MODERN CONCEPTS OF DISEASES OF THE RESPIRATORY TRACT

Early lesions of the lung even before they produce symptoms are now so readily revealed by *x* ray examination that mass chest surveys of symptomless individuals have become a part of public health measures Diagnosis of pulmonary disease can be made by other procedures in many instances but confirmation of the diagnosis usually demands *x* ray study

The internist should therefore be thoroughly acquainted with the radiologic aspects of thoracic diseases in order to have a clear understanding of the pathologic findings presented and to plan the course of therapy The radiologist must have a knowledge of the basic clinical aspects of pulmonary disease in order properly to evaluate the progress of the disease as depicted in serial films

The respiratory tract is usually considered as having two parts Diseases may affect either the upper or the lower part or both parts The upper respiratory tract consisting of the nose the nasopharynx the mouth and the larynx permits passage of air to the lungs filters out gross material and prevents its entry into the bronchi and by means of the cilia of the mucous membranes, propels to the outside mucus and other secretions collected within the airways The lower respiratory tract, consisting of the trachea bronchi lungs, and pleura has as its particular function oxygenation of the blood and removal of the carbon dioxide

Intensive research in respiratory physiology has brought about a better fundamental knowledge of pulmonary function as a guide to the medical and surgical management of the respiratory tract (*see* page 882)

Advanced knowledge of pulmonary physiology and anatomy, the development of modern methods of anesthesia and improvements in surgical technique now permit thoracotomy and resection of parts of the lung without extreme risk And recently developed diagnostic and therapeutic methods together with the basic measures which have proved effective in the past have served to reduce the mortality rate from diseases of the lung

Roentgenologic diagnosis of pathologic states within the chest are based on interpretation of shadows indicating alterations in the position or the contour of the lung or changes in the pulmonary tissues Fluoroscopy revealing disturbances of the lung's movement position or translucency also is an aid in diagnosis

When the diagnosis has not been established by simple fluoroscopy and radiology tomography (stratigraphy planigraphy laminagraphy) may be employed for localization and definition of deep-seated lesions

*Bronchoscopy* is used in diagnosis and treatment of various intrathoracic diseases It is used to determine the cause of atelectasis and the possible presence of endobronchial inflammation or new growth for the investigation of the cause of chronic cough or wheezing for aspiration of mucous plugs and bronchial secretions for cytologic study

and to obtain biopsy material *Bronchography* by utilization of radiopaque material introduced into the bronchus permits a complete survey of the bronchial tree and any existing anomalies dilatations strictures fistulas or bronchial occlusions Its use is advocated when there is suspicion of bronchiectasis or of unexplained hemoptysis, chronic cough or wheezing exists or chest *x* rays are difficult to interpret It is contraindicated if exudative tuberculosis exists the patient is debilitated hemoptysis has recently occurred the patient suffers from decreased vital capacity or thyrotoxicosis, chronic nephritis or iodine idiosyncrasy exists

Exploratory thoracotomy is a procedure used when other diagnostic measures have been exhausted

*Laboratory Procedures* —(1) One of the most important laboratory procedures in the diagnosis of tuberculosis is examination of sputum Its amount color consistency odor and content are all of significance Microscopic examination of the sputum may reveal fibers spirals polymorphonuclear leucocytes eosinophiles bronchial casts parasites, broncholiths and cancer cells

The sputum is profuse in bronchiectasis and advanced tuberculosis In the former it tends to be three layered—the top layer frothy white the bottom layer consisting of yellow pus and the middle layer fluid The sputum is frothy and tenacious in asthma rusty in pneumonia pinkish and frothy in passive congestion blood tinged in infarction bronchiectasis and tuberculosis and frankly red in hemorrhage A foul odor is noted in the sputum in bronchiectasis empyema and abscess if bacillus-coli infection is present The sputum in lung gangrene is fetid and contains tissue fragments

The sputum smear may show the presence of the colorless and hexagonal Charcot-Leyden crystals of bronchial asthma and bronchitis Dust and metallic particles in the sputum may indicate a pneumoconiosis

(2) Stomach washings may reveal the presence of tubercle bacilli in swallowed sputum Centrifuged specimens smeared on slides for microscopic study or cultured and inoculated into animals have revealed such bacilli in 90 per cent of the cases of tuberculosis with cavitation

(3) The skin tests commonly used are the tuberculin the coccidioidin and the histoplasmin If properly performed these tests are helpful in diagnosis but establish only that infection of the type tested occurred at some previous time and is not necessarily active or even recent With few exceptions a repeated negative reaction rules out the disease in question

(4) Cytologic examination of bronchial washings or sputum may reveal the presence of cancer cells when at least three separate sputa are examined such tests are quite reliable and false positives are few in number Cytologic examination of pleural transudates centrifuged at high speed and the sediment stained with Wright s stain may reveal lymphocytes whereas suppurative exudates show neutrophile leucocytes almost entirely

(5) The erythrocyte sedimentation test is frequently used as a guide to therapy and prognosis in tuberculosis an accelerated sedimentation rate after prolonged bed rest being a poor prognostic sign Sudden increase in the sedimentation rate may signify impending complications However elevation of the sedimentation rate is not pathognomonic since it is observed in many acute and chronic processes

In diseases of the chest the symptoms are not pathognomonic A symptom seeming to indicate disease of the chest may actually be an expression of involvement of another system of the body while a far advanced lung disease except for possible functional changes may produce no symptoms

*The Clinical Syndrome of Diseases of the Respiratory Tract* —The symptoms most commonly observed in pulmonary disease are cough expectoration dyspnea cyanosis chest pain hemoptysis clubbing of the fingers and toes fever and polycythemia Any or all of these symptoms may occur in a single case They are helpful to only a small degree in the differential diagnosis of pulmonary infections

*Cough* —Cough is one of the most frequent and most persistent symptoms of pulmonary infections yet it may be slight or entirely

absent in some of the most serious affections of the lung Cough is normally a protective reflex designed to expel foreign bodies, as well as obstructive accumulations of mucus, from the bronchus but it may also force infective material downward into the lung

The type of cough varies according to the infective process in the pulmonary mucous membranes Chronic coughs accompany pulmonary tuberculosis, chronic bronchitis, heart disease, asthma, emphysema and bronchiogenic carcinoma When an unexplained chronic cough develops between the ages of 40 and 65, a bronchiogenic *carcinoma must be ruled out*

A dry hacking cough is noted in obstruction of the larynx, inflammation of the vocal cords, tracheal inflammation, bronchitis bronchopneumonia, and pleurisy it is paroxysmal in pneumonitis Muffled reverberating cough occurs in emphysema becoming toneless in the senile patient A wheezy or squeaky cough is noted in bronchial obstruction and in allergic diseases A loose throaty cough occurs in tuberculosis bronchiectasis, and abscess of the lung or in suppurative processes A short, deep *painful cough may be indicative of involvement* of the parenchyma and pleura Coughing with gagging and vomiting follows inspiration of a foreign body However, coughing attended by vomiting is often psychogenic and may persist long after the initial infection has subsided

*Expectoration* —When the self-cleansing power of the pulmonary tract proves ineffective, an accumulation of exudate foreign matter and inflammatory products occurs in the lung A short hacking cough is usually enough to expel the material in mild cases

The amount and frequency of expectoration the consistency color and odor of the sputum, its content of cellular bacterial and foreign materials are all of importance in diagnosis

*Dyspnea* —Dyspnea or labored breathing indicating disturbance of the respiratory mechanism occurs in many of the pulmonary diseases but often it indicates cardiac failure as well Dyspnea means that the lungs are unable to meet the demands upon them without effort During violent exercise of course strenuous breathing is due to fatigue not to pathologic weakness Dyspnea may be caused by metabolic disturbances, circulatory diseases, and nervous disorders It is not an early symptom of tuberculosis unless there is considerable or rapid reduction of the lung volume as in massive pleural effusion or spontaneous pneumothorax in which case there is deep stertorous breathing with lengthening of the inspiratory phase In emphysema and in chronic asthma accumulation of stagnant air causes prolonged and labored expiration

*Hoarseness* is a frequent accompaniment of chest diseases, the larynx becoming *secondarily involved either by direct extension* of the infection or by involvement of the recurrent laryngeal nerve A persistent hoarseness, hoarseness that has lasted for several weeks or more without known cause, may be due to syphilis, neoplasm or tuberculosis careful study is required to determine the basic etiology

*Wheezing* results from narrowing of air passages Diffuse wheezing may be caused by asthma or cardiac conditions in which decompensation is present or in cases of left ventricular failure by pulmonary edema *Unilateral wheezing is characteristic of* neoplasm although intrabronchial foreign bodies are an additional consideration

*Cyanosis* —Cyanosis is the dusky bluish hue imparted to the skin by the accumulation of an increased amount of reduced hemoglobin in the circulating capillary blood It has been demonstrated that at least 5 gm of reduced hemoglobin per 100 cc of blood must be present before cyanosis occurs The discoloration is usually best seen in the nailbeds mucous membranes and conjunctival vessels but as the amount of reduced hemoglobin increases the cyanosis becomes evident over the entire skin surface

Any condition interfering with oxygenation of the blood may produce cyanosis Thus it may result from diminished alveolar ventilation due to an obstructed air passage atelectasis or sudden pneumothorax or from a reduced diffusion coefficient through the alveolar membrane due to pulmonary edema or interstitial pulmonary fibrosis In certain instances several factors may contribute to cyanosis For example in lobar

pneumonia the loss of a considerable number of functioning alveoli through consolidation may be combined with rapid shallow respirations enforced by a pleuritic pain to produce a marked cyanosis

Aside from pulmonary sources of cyanosis, there are the added possibilities of the removal of excessive amounts of oxygen in a stagnant bloodstream or of the shunting of large amounts of venous blood into the arterial system as in congential heart disease (For diseases of the circulation producing cyanosis *see* page 762 )

*Note* —Cyanosis due to methomeglobinemia is to be distinguished from cyanosis of pulmonary or *cardiac origin Methemoglobinemic cyanosis may* be primary or congenital hemoglobinemia (This is due to a defect in normal red-cell mechanism to reconvert methemoglobin to hemoglobin The normal ratio is 99 hemoglobin to 1 methemoglobin in congenital cyanosis methemoglobin is kept at a level of about 40 per cent) Secondary methemoglobinemic cyanosis is due to ingestion of nitrates acetophenatidin and acetanilid For detailed discussion *see*

FINCH C A Methemoglobinemia and Sulfhemoglobinemia New England J Med 1948 *239* 470

EDER H A FINCH C and McKEE R W Congenital Methemoglobinemia A Clinical and Biochemical Study of a Case J Clin Investigation 1949 *28* 265

TEPPERMAN JAY MARQUARDT ROBERT REIFENSTEIN G H LOZNER E L Methemoglobinemic Cyanosis J A M A 1951 *146* 923

EDITOR

*Chest Pain* —Pain in the chest is neither common nor significant in diagnosis of pulmonary disease but may be the symptom that first attracts the attention of the patient Its commonest causes are pleurisy neuritis fibrositis or it may originate from cardiac and abdominal disease thereby causing considerable confusion in diagnosis It may be present with or without friction rub and varies in intensity according to the degree and rapidity of the stretching of the pleura

Pain in the chest is not a measure of the severity of the pulmonary disease present since it may be absent in cases of severe involvement of the lung—the lungs and visceral pleura have no pain sense whereas the parietal pleura is intensely sensitive Irritation of the diaphragmatic pleura produces a referred pain in the neck and shoulder, where the phrenic nerve originates

*Hemoptysis* —Bloodspitting occurs to some degree in most diseases of the lower respiratory tract but the amount of blood expectorated often has no relation to the severity of the disease Fatal hemorrhage is rare Profuse hemorrhage however may occur in cases of chronic disease with lung cavitation (bronchiectasis, carcinoma, lung abscess and fibroid tuberculosis) The bleeding usually proceeds from a bronchial artery in bronchiectasis and carcinoma and from the pulmonary artery in such ulcerative affections as tuberculosis Mitral stenosis and congestive heart disease when associated with pulmonary infarction, often cause bloodspitting Hemoptysis is rarely associated with shock or severe chest pain, except during vascular crisis

*Clubbing of Fingers and Toes* —Clubbing of the fingers and the toes is often associated with pulmonary diseases The etiology is not understood but the clubbing is generally considered to be due to a disturbance of gas exchange in the capillary circulation of the digits There may also be hypertrophy *of the lower ends of the long bones or chronic* hypertrophic pulmonary osteoarthropathy In cases of lung abscess emphysema and obstruction of the air passages by a foreign body this symptom may occur suddenly It will as rapidly disappear however, when these conditions are cured

*Fever* and *malaise*, nonspecific reactions to infections and to malignancy, are of frequent occurrence in pulmonary disease

*Polycythemia* is frequently observed in *subacute and chronic pulmonary disease* and may be considered a compensatory phenomenon for the purpose of increasing the available amount of oxygen-carrying hemoglobin It is most commonly associated with extensive fibrosis and hypertropic emphysema

Pulmonary arteriovenous aneurysm is a less common cause of polycythemia

## DISEASES OF THE UPPER RESPIRATORY TRACT

By ADRIAN J DELANEY M D

THE upper respiratory tract includes the nose and nasopharynx the mouth and oro-

pharynx and the larynx. An understanding of the anatomic relations and physiologic functions of these structures will help the examiner develop a rational approach to the diagnosis and treatment of the inflammatory and neoplastic lesions encountered in them.

To see these regions adequately, the practitioner must master the use of the head mirror or a headlight with a bright focal beam. Examination of the nasopharynx, the hypopharynx and the larynx with appropriate laryngeal mirrors requires a certain amount of dexterity and considerable practice but the information obtained is worth the effort. The nasopharynx has appropriately been termed "no man's land" because of an almost universal failure to consider it in diseases of the upper respiratory tract. The reasons for this neglect are easily understood when one attempts to examine the postnasal space in an apprehensive gagging patient with a muscular tongue. Reassurance of the patient coupled with gentle firmness on the part of the physician will often be rewarded by an early diagnosis of a malignancy that would otherwise remain in obscurity until far advanced. The simple diagnostic tools of the otolaryngologist are very useful in examining the far recesses of the nose and throat.

## NOSE AND NASOPHARYNX

The nose and nasopharynx function as air conditioners for the lower respiratory tract. The vibrissae of the nasal vestibule help filter out gross foreign particles. The vascular nasal turbinates with their ciliated epithelium and slowly moving mucous blanket warm and moisten the inspired air as it passes to the nasopharynx where it strikes the baffle plate of the pharyngeal tonsils (adenoids) before being shunted downward to the larynx. The paranasal sinuses, most of which can be considered as extensions of primary ethmoid cells, hollow out the facial and cranial bones surrounding the nose. The superior maxilla, frontal, ethmoid, and sphenoid bones are thereby made lighter and less difficult to carry in man's upright position. The air spaces in these bones are considered resonance chambers by some rhinologists. The delicate ciliated epithelium lining these spaces is covered by a thin mucous blanket that is normally swept toward the natural opening of the sinuses in a perpetual house-cleaning effort. Interference with this ciliary activity by inflammatory or allergic changes may transform the resonance chambers into rigid walled cesspools that encourage the growth of anaerobes, defy drainage and lead to chronic osteomyelitis.

Inflammations of the nasal vestibule, in the form of cellulitis or furuncle, are common. The tender, warm, red nasal tip should be treated with great respect because of the ease with which inflammations in this area reach the cavernous sinus. Hot moist compresses gently applied to the inflamed nasal tip and supported by systemic antibiotic and chemotherapeutic treatment, will usually bring about resolution of the process. Surgery is seldom indicated except to lift an obstructing crust from the apex of a pointing abscess. Repeated inflammation of the entrance of the nose may be an indication of an underlying systemic condition (diabetes, anemia, *etc.*)

Acute rhinitis, or rhinosinusitis, as it should be called, is an inflammation of the mucous membrane of the nose and its extensions into the paranasal sinuses and the nasopharynx. If the mucosal and submucosal tissues of the nose alone are involved, a simple rhinitis exists. Spread of the inflammation to the paranasal sinuses is resisted by the mucous blanket and its antibacterial enzymes, but in spite of this protective device the mucous membrane of the sinuses is frequently involved in the inflammation. Extension of the inflammatory process backward into the nasopharynx will produce a nasopharyngitis. From the nasopharynx there may be contiguous involvement of the pharyngeal orifice of the eustachian tubes with progressive inflammation reaching the middle ear and mastoid cells. If the inflammation moves downward from the nasopharynx there may be involvement of the larynx and tracheobronchial mucosa producing laryngitis, bronchitis or bronchopneumonia.

Acute rhinitis is very common. It is especially prevalent in the spring and fall in the temperate zones but it prevails the year round to lesser degree in all countries of the world. This universal occurrence allows the term "common cold" to be given to the condition.

*Etiology.*—The etiology of most cases of acute rhinitis is fairly characteristic. Lower

ing of general body resistance by chilling or wetting is followed by lowering of the temperature of the nasal mucosa with vasoconstriction stasis and anoxemia of this tissue The filterable cold virus initiates the catarrhal inflammation in the epithelium and encourages secondary invasion without symptoms by the pathogenic bacteria that are usually present in the nose and throat under normal conditions These secondary invaders include the hemolytic streptococci pneumococci staphylococci hemophilus influenzae and others

*Pathology* —The pathologic picture of acute rhinitis is one of early ischemia of the mucous membrane of the nose with scanty secretion followed by acute congestion with copious watery discharge Microscopic studies by Hilding revealed early edema of the submucosa followed by infiltration of macrophages and polymorphonuclear cells The epithelial surface sloughs off and disintegrates to form part of the nasal discharge As the submucosal infiltration progresses the secretions become more purulent Reparative processes begin as early as the fifth or sixth day with regeneration of the epithelium to produce a new intact nasal mucosa

*Symptoms* —Clinically there is early general malaise headache muscle aching dryness and a scratchy sensation in the nose and throat followed in several hours by nasal stuffiness some loss of smell watery discharge sneezing lacrimation chilly sensations fatigue and slight temperature elevation The symptoms persist for from four to six days or more and slowly subside The watery discharge may cause excoriations of the nasal vestibules but may also be produced by excessive blowing and wiping of the nose The watery discharge becomes thick and purulent and finally tenacious and dried forming crusts in the nasal cavities as the condition subsides

It should be realized that acute rhinitis may be the introduction to one of the contagious diseases of childhood such as measles pertussis or chickenpox Conservatism in returning the child to school after an attack of acute rhinitis is therefore indicated Intensification of the inflammatory process at any stage or interference with the resolution of that process may lead to complications The chief complications are acute purulent sinusitis and acute otitis media

*Complications* — *Acute sinusitis* occurs during the common cold by entrance into the sinus of secondary invaders usually found in the nose The invasion of the sinus is encouraged by local abnormalities such as deviation of the nasal septum polyps, and hypertrophied nasal turbinates Forceful entry of water into the sinuses in swimming and diving will invite infection in the presence of the common cold The pathologic changes closely resemble those of the nasal mucosa in acute rhinitis The symptoms are those of the common cold at first but as the nasal stuffiness and discharge subsides the purulent sinus discharge appears at the nares and in the postnasal space where it may cause rawness in the nasopharynx and laryngeal irritation with hoarseness and coughing Headache is common fever and malaise occur and there may be tenderness over the maxillary antrum or frontal sinus The treatment of acute purulent sinusitis consists in drainage with an isotonic vasoconstrictor such as neosynephrine or ephedrine in physiologic salt solution relief of pain with analgesics such as the salicylates and codeine and systemic therapy with antibiotics or chemotherapeutic agents as indicated

*Acute otitis media* as a complication of the common cold, usually results from the spreading of inflammation up the eustachian tube and into the middle ear Sneezing forceful blowing of the nose nasal douching swimming and diving may act as inciting agents The pathologic changes in the middle ear may be minimal with congestion and edema of the subepithelial layers and serous discharge or the epithelium may become swollen and the submucosa infiltrated with cells of inflammation leading to pus formation The symptoms are characteristic There is early fulness and pressure in the ear followed by mild sharp pains that increase in severity if the pressure in the middle ear is not relieved by spontaneous perforation or paracentesis Fever varies from 101° F in mild cases to 103 or 104 F in severe purulent involvements Deafness is present to some degree There is usually general malaise headache and anorexia In infants

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there may be vomiting and convulsions Examination of the ear reveals early injection of the eardrum along the hammer handle and at the periphery Later, the entire drum becomes reddened and injected, with loss of landmarks and normal sheen Bloody discharge or bulging may be seen in the posterior portion Mastoid tenderness is a warning sign of further spread This complication of the common cold demands the use of systemic chemotherapy or antibiotics, local use of heat mild analgesics, and supportive therapy including bed rest Consultation with an otologist should not be delayed if the symptoms and signs are progressive

*Treatment* of acute rhinitis is not specific Early bed rest and isolation of the patient are good advice and help prevent the spread of colds Salicylates alone or combined with codeine or papaverine, will relieve headache and muscular pains A combination of papaverine and codeine, one fourth grain of each, may shorten the course of the cold The drinking of fluids in the form of fruit juices, water, or carbonated beverages should be encouraged, and the diet should be light and easily digested Nasal discomfort may be relieved by a mild vasoconstrictor such as ½ per cent neosynephrine or ephedrine in physiologic salt solution Steam inhalations may give symptomatic relief A mild laxative is indicated if a tendency toward constipation has preceded the onset of the rhinitis The use of antibiotics or chemotherapeutic agents in the treatment of uncomplicated acute rhinitis is not indicated

## MOUTH AND OROPHARYNX

The mouth and oropharynx should be considered together since any inspection of the throat or pharynx must necessarily include the mouth (For a discussion of Diseases of the Oral Cavity *see* Chapter 27 )

### Acute Pharyngitis

Acute catarrhal pharyngitis is a generalized inflammation of the mucous membrane of the pharynx It may be the initial stage of acute rhinitis or sinusitis or of an acute inflammation of the lower respiratory tract Sometimes it occurs with an acute stomatitis

*Etiology*—The etiologic agent is usually the hemolytic streptococci, although staphylococci, pneumococci, streptococcus viridans and influenza and colon bacilli have been inciting or contaminating agents in many cases That a virus is the cause of the condition has not been proved The onset of acute pharyngitis is encouraged by a lowering of the general body resistance by alcoholic excess chilling, constipation or exhaustion from overwork The condition begins with dryness, soreness and burning in the throat, discomfort in swallowing tender enlarged cervical lymphnodes low grade fever, malaise generalized muscle aching and headaches Thick, tenacious secretion is produced in excess and causes much hawking and rasping as the patient tries to expectorate

*Pathology* —The pathologic picture is one of acute congestion of the mucous membrane of the pharynx increased secretion of the mucous glands producing a copious thick saliva and a lymphoid type of cellular infiltration of the epithelial tissues especially around the dilated blood vessels and glands

The diagnosis is based on the characteristic appearance of the bright red congestion of the entire pharynx thick sticky mucus and mild local and general symptoms Acute catarrhal pharyngitis could be the prodromal stage of an acute contagious disease such as measles scarlet fever poliomyelitis or meningitis If the condition fails to respond to simple treatment more serious diseases such as these must be suspected Acute infectious mononucleosis or agranulocytic angina may be confused with simple acute pharyngitis unless blood smears are studied

*Treatment* —The treatment of acute pharyngitis is similar to that recommended for acute rhinitis (*see page 870*) *Local therapy* with warm mild alkaline mouth washes and gargles or irrigations an ice collar for the neck anesthetic throat lozenges and soothing nose drops may be advised *Topical* applications of antiseptics are made useless by the abundant thick secretions that prevent adherence of the medication to the mucous membrane

### Chronic Pharyngitis

Repeated attacks of acute pharyngitis or rhinitis may lead to chronic pharyngitis This condition is characterized by constant or repeated intermittent episodes of dryness and rawness of the throat which is almost constantly sore The pathologic features of importance are thickening of the epithelium dilatation of capillaries perivascular round-cell infiltration of the vessels of the subepithelial tissues and dilated mucous glands

*Signs and Symptoms*—There are abundant, thick tenacious mucous secretions with resultant hawking or coughing and a general feeling of malaise Examination of the throat reveals a dull red velvety thickening of the mucous membrane thick yellowish green adherent secretions and a glazed dull red appearance of the posterior wall of the pharynx

*Treatment*—Treatment of chronic simple pharyngitis is difficult The underlying cause or causes must be searched for and removed if possible Chronic infection in the sinuses or tonsils should be eradicated Systemic conditions such as diabetes nephritis and constipation must be sought for and treated appropriately Chronic abuse of alcohol and tobacco must be forbidden A well rounded diet adequate rest and appropriate open air exercise are basic requirements Full cooperation of the patient is absolutely necessary to effect a satisfactory cure Local therapy with nasal and throat irrigations with saline or mild alkaline solution is sometimes beneficial Stimulating menthol throat lozenges are helpful Removing the secretions and swabbing the inflamed areas with Mandl s iodine solution is good office treatment Systemic chemotherapy and antibiotics are seldom necessary

### Acute Tonsillitis

Acute tonsillitis is a very common affliction frequently undiscovered because the inflammation affects a portion of the pharyngeal lymphoid structures that is not seen in the routine examination Actually there are several lymphoid masses or tonsils in the pharynx In the roof of the pharynx called the nasopharynx the pharyngeal tonsils or *adenoids* are located In childhood the poorly encapsulated masses occupy the mid line of the vault of the pharynx and spread laterally into the recesses of the vault the fossæ of Rosenmuller In this location the lateral extensions of the adenoids may impinge on the pharyngeal openings of the eustachian tubes and interfere with normal exchange of air between the nasopharynx and the middle ear In such cases inflammation of the adenoids may cause repeated attacks of otitis media Deafness of a perception type is commonly caused by hypertrophied adenoid tissue in this region even after adenoidectomy has been performed It is in such cases that the use of radium or roentgen irradiation is advisable to reduce the localized adenoid hypertrophy Below the nasopharynx in the lateral gutters of the pharynx are often found linear masses of lymphoid tissue extending from the eustachian tube openings down behind the posterior pillar of the tonsil and into the hypopharynx where they gradually disappear These masses are seen more commonly following conventional tonsillectomy especially in persons with frequent head colds and postnasal discharge They are so familiar to the otolaryngologist that the name *lateral bands* has been applied to them

In addition to these masses there are two distinct pairs of *tonsils* the faucial and lingual The faucial tonsils have definite boundaries and are located at the vestibule of the pharynx between the anterior and posterior pillars or folds of the fauces The lingual tonsils are situated on the base of the tongue in front of the tip of the epiglottis The faucial tonsils are well known to all physicians and are readily examined The lingual tonsils however are given scant attention by most practitioners because they must be examined by palpation with the finger tip or by drawing the tongue out of the mouth and using a laryngeal mirror This latter maneuver frequently requires time and patience because of the patient s gagging and involuntarily withdrawing the tongue

The four masses of superficial lymphoid tissue in the nasopharynx and the pharynx —the adenoids the lateral bands the faucial tonsils and the lingual tonsils—make up the ring of Waldeyer All may become involved

in inflammation at one time in such conditions as *infectious mononucleosis and diffuse* pharyngeal diphtheria More often, however, one or more of the masses will become hypertrophied or inflamed

*Etiology* —The etiologic agent in acute tonsillitis is *probably a virus in most cases* The hemolytic streptococcus is the offending organism in about 25 per cent of the cases especially when the constitutional symptoms are severe and complications are common *Predisposing factors are chilling of* the body excesses in eating and drinking fatigue and constipation

*Pathology* —The pathologic picture is the same whether found in the adenoids, faucial tonsils, *lingual tonsils or lateral bands* There is a superficial loss of epithelium serous discharge exudation of polymorphonuclear cells from the capillaries edema of the submucosa and congestion of the blood vessels As the process advances there is erosion and ulceration of the submucosa The tonsillar crypts become filled with fibrin desquamated epithelium pus cells and bacteria to produce the yellowish spots on the surface

*Symptoms and Signs* —When the faucial tonsils are involved in acute tonsillitis the symptoms are classical When the adenoids are involved rawness scratching sensations in the postnasal space and nasal speech described as rhinolalia are characteristic When the lymphoid masses in the lateral gutters are involved painful swallowing is especially troublesome When the lingual tonsils are inflamed a sharp stabbing pain in the region of the hyoid bone accompanies swallowing and some dyspnea or hoarseness may be present The patient complains of a lump in the throat

Clinical symptoms of acute tonsillitis begin with a chill *a temperature of 101 to* 104° F headache malaise aching pains in the back and in the extremities painful throat, and anorexia In infants a convulsion may mark the onset of this condition At first the throat is dry then pain on swallowing is noted and, as the inflammation advances there is increasing difficulty in swallowing painful hawking of thick tenacious mucus muffled voice painful enlarged cervical lymphnodes heavily *furred tongue and bad breath*

Examination reveals redness and congestion of the mucous membrane of the pharynx, most marked on the faucial tonsils and the tonsillar pillars The tonsils are swollen *angry red in appearance with yellow or* yellowish white membrane plugging a few or many of the pouting tonsillar crypts The membrane can be removed with relative ease leaving a raw, but not bleeding, base *and often releasing fluid pus from the plugged* crypts If the hemolytic streptococcus is the causative agent there are likely to be intense edema of the tonsillar pillars soft palate and uvula more widespread *membrane formation marked enlargement* and tenderness in the cervical lymph nodes and more severe constitutional symptoms

*Differential Diagnosis* —In the differential diagnosis all conditions characterized by membrane formation in the pharynx must be considered These include diphtheria fusospirochetal pharyngitis thrush infectious mononucleosis and agranulocytosis In children there is always the possibility that an acute sore throat may be an early symptom of scarlet fever measles or meningitis

*Treatment* —Treatment of acute tonsillitis involves bed rest isolation chemotherapy or antibiotic therapy relief of pain and discomfort through the use of analgesics local treatment of the involved tissues and a close watch for impending complications Before any definitive therapy is instituted smears and cultures should be taken to rule out diphtheria and also to identify the causative organism if treatment is not effective It is probably justifiable in severe acute tonsillitis to use full doses of antibiotics as soon as cultures have been taken from the tonsillar membrane even though their effect on a virus is questionable If the secondary invaders present in the pharynx are prevented from disseminating antigen in the circulating blood by antibiotics or chemotherapy the occurrence of such allergic complications as nephritis rheumatic fever or rheumatoid arthritis may be decreased Local therapy in the form of warm saline irrigations soothing medicated lozenges and an ice collar applied to the swollen tender lymphnodes of

the neck will provide some relief An easily digested liquid diet should be offered the first day or two this to be followed by a semi soft diet and then full diet as the dysphagia subsides

### Chronic Tonsillitis

Chronic tonsillitis usually results from repeated attacks of acute tonsillitis the faucial tonsils frequently are primarily involved but the same low-grade chronic inflammation may produce prolonged congestion in any or all of the lymphoid structures that make up Waldeyer s ring In the clinical picture of chronic tonsillitis the tonsil pillars show constant dull redness and congestion accentuated throughout the length of the medial margins The tonsils themselves may be large or small but are usually dull red in color and slightly congested They present several small whitish gray areas of fibrous tissue infiltration resulting from previous acute inflammations Usually one or two enlarged slightly tender lymphnodes occur below the angle of the mandible There is a definite history of repeated attacks of acute tonsillitis often a peritonsillar abscess and frequent head colds There is only one treatment for chronic inflammation of the faucial tonsils—tonsillectomy If the lingual tonsils or the adenoids are chronically inflamed they will present the same sort of appearance as the faucial tonsils and there will be a history *of repeated head colds and sore throat* With adenoid involvement repeated attacks of otitis media with residual deafness can be expected Lingual tonsillitis may cause repeated attacks of simple laryngitis Both conditions will cause excessive amounts of secretions in the pharynx leading to chronic hawking coughing and rasping of the throat Both conditions may be cured by surgical removal of the offending lymphoid masses or by radiation therapy with *x* ray or radium as indicated by the location of the tissue to be treated

It should be remembered that the tonsils and adenoids are frequently invaded by malignant neoplasms especially lymphoepithelioma and lymphosarcoma both of which may cause rapid enlargement of these structures and the regional cervical lymph nodes Such cases should be referred to an expert irradiation therapist as soon as possible

## LARYNX

The larynx is situated just below the pharynx it is in front of the opening of the esophagus and at the top of the tracheobronchial tree At the top the larynx opens widely into the lower pharynx or hypopharynx and at the bottom is continuous with the trachea The larynx may be invaded by inflammatory or neoplastic lesions rather extensively without producing any symptoms It is only when the vocal cords are involved or the glottic airway is encroached upon that the characteristic symptoms of hoarseness and air hunger are elicited Pain is not often complained of unless the perichondrium of one of the laryngeal cartilages is acutely inflamed Inflammation of the larynx especially in infants and young children may progress very rapidly in spite of all treatment so that emergency measures such as tracheotomy or intubation are required early For this reason it is wise to treat these cases in a well-equipped hospital whenever possible Neoplasms of the larynx are fairly common They should be suspected in all cases of hoarseness of over 10 days duration For all practical purposes it is well to assume that there is no such disease as chronic laryngitis until it has been *proved by histopathologic studies of tissues* removed at laryngoscopy by an experienced laryngologist

Acute laryngitis is an acute inflammation of the laryngeal mucosa it is usually widespread in all parts of the larynx It is often associated with the common cold or with an acute exacerbation of a chronic sinusitis The characteristic symptoms are a rough and rasping voice progressing to a rough whisper or even to complete aphonia tickling and dryness in the region of the larynx a dry hacking cough and a slight soreness in the larynx Examination reveals a diffuse redness of the laryngeal mucosa with dilated superficial vessels and thick dry mucous secretion Constitutional symptoms are never more than slight The condition responds

rapidly to voice rest and body rest steam inhalation and avoidance of dusty environments and raw, damp atmospheres The use of finely divided aerosol sprays of Mono-P-*chlorphenol or of gomenol may add to the* patient s comfort

Chronic laryngitis is long continued inflammation of the laryngeal mucous membrane It follows repeated acute attacks, especially when these are secondary to chronic infection in the sinuses or nasopharynx Chronic irritation resulting from tobacco smoke industrial fumes or a dusty environment may predispose to chronic inflammation The voice is rough with a lower pitch than normal vocal fatigue is common There is cough and much hawking to remove sticky secretions On examination the entire mucosa looks a dull velvety red and shows some thickening of the false vocal cords and often of the true vocal cords Treatment is not effective unless the underlying cause is found and eliminated If no cause can be found, malignancy must be suspected

Edema of the larynx may occur as a complication of acute or chronic laryngitis It is seen in phlegmonous inflammations of the floor of the mouth or deep fascial spaces of the neck It may be associated with edema elsewhere in the body as in nephritis or angioneurotic edema The onset is often sudden, causing respiratory embarrassment whispering hoarseness stridulous respiration and panicky asphyxia requiring tracheotomy Mirror examination shows boggy swelling of the entire laryngeal mucosa including the epiglottis and aryepiglottic folds Expert handling is required to avoid asphyxial death If the edema cannot be *reduced by systemic therapy or surgical* drainage of paralaryngeal fascial spaces tracheotomy must be performed

Tuberculous laryngitis is usually secondary to pulmonary tuberculosis but may be primary Slight huskiness of the voice is common in pulmonary tuberculosis, when it becomes marked the larynx should be carefully examined for ulceration, especially if pain is marked If the epiglottis is involved painful deglutition occurs If the cords are ulcerated pain is experienced during phonation The most usual sites of early lesions are the posterior commissure and arytenoid cartilages The mucous membrane is pale in the early stages but later thickens and turns deep red Restricted movements of the vocal cords may be noted If the infection is limited to the intrinsic larynx it usually runs a slow course and is amenable to treatment Involvement of the epiglottis and *arytenoids however, may signify* a rapidly progressive infiltration with extensive ulceration and sloughing off of tissues this offers a poor prognosis Treatment consists of absolute bed rest and voice rest Analgesic sprays help relieve pain Streptomycin given systemically and locally in the form of aerosols, is almost a specific In severe pain, alcohol injection of both *superior laryngeal nerves gives prolonged* relief Quartz ultraviolet light, applied to the larynx by means of special apparatus, is sometimes useful The pulmonary lesions must be brought under control before the laryngeal lesions will become fully quiescent

Syphilis of the larynx is usually seen in the tertiary stage although secondary lesions of the larynx sometimes occur concomitantly with the pharyngeal erythema and the mucous patches of the mouth Primary chancre may be seen on the epiglottis under rare conditions The usual lesion is an infiltration of the entire larynx involving especially the epiglottis and false vocal cords There is a deep red nodular involvement of the mucosa and submucosal tissues this may so progress as to form deep punched out gummatous ulcers unless specific therapy is instituted Serologic tests are usually strongly positive Antiluetic treatment brings prompt improvement

*Cancer of the larynx occurs most fre*quently in the sixth decade in males Epidermoid carcinoma of the true cords is the usual form The earliest warning symptom is hoarseness Pain is often a late symptom *followed by dry cough and hemoptysis* Mirror examination in the early stages may reveal rough thickening of the anterior third of a vocal cord or of the anterior commissure Limitation of movement of the involved cord is a late sign As the disease progresses it spreads locally to involve the entire larynx on the side of origin, and then spreads to the

opposite side Metastatic spread to the cervical lymphnodes is a bad prognostic sign indicating a late stage of the disease The key to the early diagnosis of cancer of the larynx is the maintenance of a high index of suspicion on the part of every practitioner who treats a patient over fifty with hoarseness of 10 days duration All suspicious lesions seen on mirror examination should be biopsied Early lesions confined to one vocal cord are successfully treated surgically in a high percentage of cases with preservation of good phonation Advanced cases require laryngectomy often accompanied by radical dissection of the deep lymphnodes in the neck to relieve pain and allow a chance of cure X ray therapy has its greatest chance of success in highly anaplastic lesions

The larynx is the vestibule of the tracheobronchial tree which consists of the trachea the right and left main bronchi and the secondary and tertiary bronchi The entire laryngotracheobronchial tree can be seen by endoscopy, this method of direct examination has developed rapidly in recent years It is no longer considered a special method of examination which can be performed only by highly trained specialists in large clinics Today endoscopic examination of the larynx trachea and bronchi is second in importance only to $x$ ray examination of the lung in the study of pulmonary disease The interpretation of $x$ ray findings is frequently made with much greater accuracy after the endoscopic examination has been reported The exact localization of isolated lesions of the lungs is made possible by supplementing roentgen visualization with bronchoscopic studies

*Endoscopic Examination of the Tracheobronchial Tree* —In the hands of an experienced manipulator bronchoscopy is neither difficult nor dangerous Usually it is performed under local anesthesia following premedication with morphine and cocaine Sedation is sometimes required to ensure adequate relaxation Hospitalization is unnecessary for most patients since the procedure seldom entails collapse or shock and never produces trauma unless it is unduly protracted or improperly executed

There are certain affections of the respiratory tract for which the endobronchial method seems particularly well adapted for nonsurgical diagnosis and treatment They are chiefly, atelectasis resulting from thick pulmonary secretions bronchiectasis bronchial stenosis, asthma pulmonary abscess malignancy of the lungs, persistent hemoptysis of obscure origin and tuberculosis Each of these conditions of the chest will be considered elsewhere

Pneumonography with bismuth subcarbonate or with a radiopaque substance in oil represents a valuable adjunct to bronchoscopy for the exploration of the tracheobronchial tree in certain instances The instillation of an oily solution may be effected by bronchoscopy, and bronchoscopic pneumonography may be practiced on a fluoroscopic table with the bronchoscope left in position while roentgenograms and fluoroscopic observations are completed Or the opaque medium may be introduced by a laryngeal cannula or catheter The iodized oil may be removed by aspiration through the bronchoscope Cough and postural drainage should be induced immediately following the conclusion of the study Patients should be cautioned not to swallow expectorations which may contain oil

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## REFERENCES

*Diseases of the Upper Respiratory Tract*

BLAIR, V P and IVY R H Essentials of Oral Surgery St Louis C V Mosby Company 1944 I 66 216

BOIES L R Fundamentals of Otolaryngology Philadelphia W B Saunders Co 1949 147 273

DIEHL, H S Medicinal Treatment of the Common Cold J A M A 1933 *101* 2042

HILDING A C Summary of Some Known Facts Concerning the Common Cold Ann Otol Rhin and Laryng 1941 *53* 444

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## REFERENCES

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REFERENCES

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Diehl H S Medicinal Treatment of the Common Cold J A M A 1933 *101* 2042

Hilding A C Summary of Some Known Facts Concerning the Common Cold Ann Otol Rhin and Laryng 1944 *53* 444

JACKSON C and JACKSON C L Diseases of the Nose Throat and Ear Philadelphia W B Saunders Company 1945 1 416
MORRISON, W S Diseases of the Ear Nose and Throat New York Appleton Century Crofts 1948, 275
PEABODY J W Bronchoscopic Aids in Medical Conditions Within the Chest Dis Chest 1943 9 307

## DISEASES OF THE BRONCHI

By J WINTHROP PEABODY M D and J WINTHROP PEABODY JR M D

### ACUTE BRONCHITIS

*Definition and Etiology* —Acute bronchitis or tracheobronchitis, is a catarrhal inflammation of the bronchi Usually it also involves the trachea Though it may be a primary inflammation it commonly results from the spreading of an infection from the upper respiratory tract into the trachea and bronchi It may follow a neglected cold acute rhinitis sinusitis, tonsillitis or pharyngitis Not infrequently it develops as a direct result of diphtheria trichinosis coccidioidomycosis, or irritating gases The contributing factors are often exposure to cold or dampness chilling, fatigue and malnutrition Bronchitis is usually a mild disease unless accompanying a more serious affection such as grippe influenza, measles whooping cough allergic diseases or virus pneumonia The very young the debilitated and the aged are particularly liable to the disease and in these it may become serious

*Clinical Features* —The earliest symptoms of acute bronchitis are a feeling of malaise and tightness or pain in the chest attended by a dry distressing cough Expectoration of mucus brings some relief The cough loosens and the mild fever subsides in a week or ten days If the case is more severe the breathing is asthmatic the cough loud and barking and symptoms may last for several weeks Bronchopneumonia often follows

Physical examination may reveal no abnormal physical signs over the chest if only the trachea and the large bronchi are involved Usually expiration is prolonged with dry wheezing rhonchi are heard as the mucous membranes of the medium sized and smaller bronchi become inflamed and swollen Moist rales are heard as the secretion increases and the expiratory murmur is prolonged as the air passages become partly clogged with mucus As the smaller ramifications become involved high pitched tubular breathing may be noted over the collapsed areas of the lung The tracheal and bronchial membranes are red and swollen and as the disease progresses become velvety in texture The ciliated epithelium is damaged The membranes return to normal with recovery In the uncomplicated case fluoroscopic and radiographic examination are negative

*Differential Diagnosis* —It is necessary to establish whether the acute bronchitis is the sole condition present or is a local manifestation of another disease In children, foreign bodies enlarged mediastinal lymphnodes whooping cough and measles must be ruled out Tuberculosis should be ruled out by radiologic studies and bronchiectasis by bronchographic examination when cough fever and malaise persist Pneumonia is to be suspected when the temperature and the pulse and respiratory rates are elevated

*Treatment* —Prophylactic measures such as avoidance of exposure prevention of contact with known cases of bronchitis and isolation of the patient are important Treatment involves bed rest warm air a bland diet high intake of fluids and keeping the bowels open Small doses of sedatives expectorants and codeine mustard poultices and steam inhalations bring relief especially when the cough is paroxysmal and irritating If there is an associated asthma difficult breathing may be relieved by administration of adrenalin or ephedrin The treatment of the infection should continue even into the convalescent period to prevent development of bronchopneumonia The sulfonamides and penicillin have been found ineffective but good results have been reported in some cases from use of aureomycin Usually antibiotics are not indicated

*Prognosis* —If the bronchitis is associated with a concurrent upper respiratory tract infection the symptoms become more serious and may abate and recur from time to time Mucous plugs may lead to occlusion of the bronchi and collapse of the lung Repeated

attacks of acute bronchitis rarely cause chronic bronchitis

*Acute Laryngotracheobronchitis* —Acute laryngotracheobronchitis occurs most often in children The onset is sudden with inflammation of the membranes severe cough, dyspnea and cyanosis A thick tenacious exudate later appears this becomes gummy and purulent obstructs the bronchial tree and causes atelectasis Distention of the alveoli may lead to mediastinal emphysema and pneumothorax Bacteriologic study will distinguish the disease from laryngeal diphtheria and laryngismus stridulus The clinical picture may be confused with that of bronchopneumonia Tracheotomy or bronchoscopy may be required to relieve the respiratory embarrassment and remove the crusty exudates Oxygen therapy and antibiotic treatment (parenterally and by aerosols) should be employed Morphine is contraindicated Unless prompt and adequate therapy is administered the prognosis is grave

*Ulcerative Tracheobronchitis* —Ulcerative tracheobronchitis which often follows pulmonary abscess sarcoidosis and fungous infections is attended by a persistent cough with blood tinged expectoration and some fever The diagnosis is dependent upon bronchoscopic evidence of ulceration and a history of one of the etiologic diseases Treatment is dependent upon the causative agent

## Chronic Bronchitis

*Definition* —Chronic bronchitis may be defined as prolonged inflammation of the mucous membranes of the bronchi their divisions and subdivisions with a tendency to exacerbation after periods of quiescence The majority of the sufferers are in the late decades of life They have persistent cough during the winter or frequent colds that defy treatment

*Etiology* —Predisposing factors are as follows (1) Lowered resistance Resistance is lowered by chills exposure to dampness fatigue undernourishment debility from recent disease or such local factors as mouth breathing excessive smoking and continued exposure to dusts and fumes (2) Cardiac insufficiency This causes poor oxygenation of the blood and so reduces ciliary defense efficiency (3) Maldevelopment of the chest (4) Chronic pulmonary diseases such as tuberculosis silicosis *etc* (5) Age (6) The microorganisms responsible for chronic bronchitis are (1) fungi and such specific bacteria as tubercle bacilli and (2) the microorganisms usually found in the respiratory tract

*Pathology* —Chronic bronchitis may be hypertrophic or atrophic In the hypertrophic stage hypertrophy of the bronchial wall and thickening of the mucous membrane are noted The mucous secretion is more copious than in acute bronchitis and may be mucoid mucopurulent or purulent In the milder form of the disease the mucosa is chiefly involved but as the bronchitis progresses the deeper layers and peribronchial areas are affected with thickening of the bronchial fibrous tissues and the interstitial septa If the weakened wall yields to pressure bronchiectasis develops

In the atrophic stage gradual disappearance of the bronchial mucous glands and bronchial elastic and muscular tissue is noted

*Symptoms* —The symptoms of chronic bronchitis differ from those of acute bronchitis in degree and duration Cough is the principal symptom A persistent cough is the rule It is usually worse in the morning and is always worse in cold or changeable weather The sputum varies in amount It may be tenacious and scanty so that it is dislodged with difficulty, or copious and semipurulent Sputum streaked with blood is rare unless there is an associated bronchiectasis Dyspnea a frequent symptom increases with the duration of the disease and when severe usually indicates associated cardiac failure or pulmonary fibrosis and emphysema Chest pain is rare

*Signs* —The signs of chronic bronchitis vary depending on the infective agent and on whether the bronchitis is wet or dry In the dry type lung resonance is generally normal dry rhonchi may be heard throughout the chest In the wet type moist rales are noted During acute attacks fever may or may not be present and there is an increase in sputum rales and rhonchi However an afebrile course is not unusual Cyan

osis, when present indicates underlying serious cardiac or pulmonary disease

In asthmatic bronchitis, high pitched musical râles at the end of expiration are noted

*Diagnosis* —The diagnosis of chronic bronchitis is based on the history signs, symptoms, and determination of the underlying cause If the patient has had a chronic productive cough for years without evident impairment of general health and examination fails to reveal evidence of any specific disease in which chronic cough is a predominant feature the diagnosis is established

The sinuses should always be investigated for a causative focus of infection Other foci should be sought in the lung (bronchiectasis cystic disease abscess or cancer) Examination of the sputum may reveal the presence of various organisms such as micrococcus catarrhalis pneumococci streptococci both hemolytic and nonhemolytic, streptococcus viridans Friedländer's bacilli and staphylococci

Roentgen examination is unrevealing in early cases but in patients with recurrent attacks over a period of years striations due to linear fibrosis may be observed in the lungs

*Treatment* —Therapy consists largely in keeping the patient away from unfavorable environments If the patient can afford to reside in a dry locality not subject to abrupt changes in temperature or to excessive cold he may live in considerable comfort The underlying cause of the bronchitis must first be found, of course and eliminated insofar as possible The treatment is entirely medical and is prophylactic and symptomatic The patient should be protected against temperature changes should stay indoors during inclement weather, should wear warm clothing, and above all should be protected against infectious diseases His general resistance should be improved by high caloric high vitamin diet and a reduction in use of alcohol and tobacco A slowing down of pace, with restful days and nights is desirable especially for the older patients

Drugs are administered for relief of symptoms The troublesome cough may be relieved by use of expectorants to liquefy the sputum Potassium or sodium iodide are widely recommended If the *cough* is exhausting small doses of codeine may be necessary Cough should not be controlled however to the extent that the cough reflex is so repressed as to prevent necessary expectoration Postural drainage should be practiced when the raising of sputum proves troublesome Ephedrine which is particularly helpful in bronchospasm, may prove toxic in the aged Other *bronchodilators*, such as orthoxine hydrochloride given orally and isuprel, sublingually, have been found beneficial

Vaccine therapy has proved disappointing Penicillin aerosolization has proved to be a valuable adjunct Deep inhalation of 100 000 units of penicillin dissolved in 3 cc of physiological saline or 1 1000 aqueous solution of zephyran, every 6 to 8 hours for approximately 10 days often results in symptomatic improvement In asthmatic bronchitis nebulization solutions are helpful Richards Barach and Cromwell recommend a mixture of vaponefrin (1-to-100 epinephrine) with or without 1 per cent neosynephrine, in a nebulizer and a flow of from 1000 to 6000 cc of oxygen per minute passed through it from a pressure tank Use of aerosol antibiotic therapy in treatment of chronic bronchitis may produce striking palliative results and occasionally, lasting cures

*Prognosis* —Prognosis depends on control of the underlying disease maintenance of general good health and prevention measures If the patient must remain in an unfavorable environment the prognosis is not good If he is economically able to live in a temperate dry climate he may live in fair comfort for years

## Rare Forms of Bronchitis

*Fibrinous bronchitis* (plastic bronchitis) is an uncommon form of the disease in which tough fibrinous casts formed in the bronchi are ultimately coughed up It may be acute or chronic and may last for years It may be a primary infection or one associated with pulmonary tuberculosis or asthma In its acute form fever pain in the chest cough and dyspnea may occur Expectoration of the casts results in disappearance of symp-

toms Expectorants and supportive measures provide the best therapy

*Bronchiolitis fibrosa obliterans* results from inhalation of irritating gases the symptoms are cough dyspnea and cyanosis The bronchioles are obliterated by obstructive epithelial cells and overgrowth of connective tissue Sedation and continuous oxygen administration constitute treatment

*Spirochaetal bronchitis* is a hemorrhagic bronchitis characterized by the presence of spirochetes in the sputum The symptoms are cough mucopurulent sputum occasional hemoptysis and fever It is a disease rarely noted in this country except in those who have visited the Orient and may be mistaken for pulmonary tuberculosis It can be diagnosed only on sputum examination Arsenic is considered specific for this disease and arsphenamine or mapharsen is usually employed

## Bronchiectasis

*Definition* —Bronchiectasis is a chronic disease characterized by dilatation of the bronchi or bronchioles with pathologic changes in the bronchial walls and adjoining tissues It is due to an inflammatory process and is generally associated with chronic broncho-pulmonary suppuration The patient may long be unaware of its presence or may have symptoms so severe as to be a lifelong invalid or semi invalid The disease is often diagnosed as chronic bronchitis unresolved pneumonia pulmonary abscess pneumonitis or tuberculosis

*Etiology* —Bronchiectasis may be congenital or acquired Congenital bronchiectasis is uncommon It may be associated with situs inversus cystic fibrosis of the pancreas or other congenital anomalies Most cases of bronchiectasis are acquired

The etiology of acquired bronchiectasis remains controversial The principal theory is that mechanical dilatation of the bronchi is followed by weakening of the bronchial walls and failure of adequate drainage with resultant infection of the bronchi Pathologic changes in the bronchial tree are thus brought about by retention of the exudate with further obstruction and infection Bronchial dilatation therefore is not the sole cause of bronchiectasis It is only when such dilatation is accompanied by inadequate drainage facilities and formation of a plug of normal secretions and exudates that bronchial infection and its symptoms are manifested The initial cause of the disease may be the presence of foreign bodies broncholiths bronchopleural fistulas pneumoconiosis enlarged lymphnodes and tuberculous fibrosis Although broncho-pneumonia is considered a precursor of bronchiectasis virus pneumonia is not believed to be an etiologic agent although cases of "psuedo-bronchiectasis" temporary bronchial dilatation have been described in virus pneumonia Infectious diseases such as measles or whooping cough may cause a bronchiectasis Thus any bronchial infection of infancy or childhood may be followed by atelectasis, pneumonitis bronchitis, and finally, bronchiectasis

Sinusitis may precede accompany or follow bronchiectasis but few believe that bronchiectasis is secondary to paranasal sinus infection

Bronchiectasis secondary to tuberculosis is a relatively frequent pathologic finding and is often unrecognized It results from a combination of bronchial and pulmonary factors Tuberculous lesions of the bronchi with associated peribronchial obstruction produce interference with pulmonary ventilation and drainage with resultant retention and stagnation of secretions Chronic pulmonary fibrosis produces loss of elastic tissue and reduction of lung volume Another factor often unappreciated is the effect of tuberculous caseous pneumonia or bronchopneumonia which by decreasing aerated parenchyma and distensibility lowers intrathoracic pressure and exerts traction on the bronchial wall producing ectasia

*Pathology* —The essential process in bronchiectasis has been described as an ulcerative lesion in the bronchi with destruction of the epithelium muscle and elastic fibers of the bronchi and frequent extension of the destructive process into the surrounding tissues of the lung This process is furthered by stenosis of the bronchus a stenosis causing retention of infective secretions and weakening of the elastic tissues resulting in dilatation of the bronchial walls Two main types

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*Etiology.*—Bronchiectasis may be congenital or acquired. Congenital bronchiectasis is uncommon. It may be associated with situs inversus, cystic fibrosis of the pancreas or other congenital anomalies. Most cases of bronchiectasis are acquired.

The etiology of acquired bronchiectasis remains controversial. The principal theory is that mechanical dilatation of the bronchi is followed by weakening of the bronchial walls and failure of adequate drainage with resultant infection of the bronchi. Pathologic changes in the bronchial tree are thus brought about by retention of the exudate with further obstruction and infection. Bronchial dilatation, therefore, is not the sole cause of bronchiectasis. It is only when such dilatation is accompanied by inadequate drainage facilities and formation of a plug of normal secretions and exudates that bronchial infection and its symptoms are manifested. The initial cause of the disease may be the presence of foreign bodies, broncholiths, bronchopleural fistulas, pneumoconiosis, enlarged lymphnodes and tuberculous fibrosis. Although broncho-pneumonia is considered a precursor of bronchiectasis, virus pneumonia is not believed to be an etiologic agent, although cases of pseudo-bronchiectasis, temporary bronchial dilatation, have been described in virus pneumonia. Infectious diseases such as measles or whooping cough may cause a bronchiectasis. Thus any bronchial infection of infancy or childhood may be followed by atelectasis, pneumonitis, bronchitis and finally, bronchiectasis.

Sinusitis may precede, accompany or follow bronchiectasis but few believe that bronchiectasis is secondary to paranasal sinus infection.

Bronchiectasis secondary to tuberculosis is a relatively frequent pathologic finding and is often unrecognized. It results from a combination of bronchial and pulmonary factors. Tuberculous lesions of the bronchi with associated peribronchial obstruction produce interference with pulmonary ventilation and drainage with resultant retention and stagnation of secretions. Chronic pulmonary fibrosis produces loss of elastic tissue and reduction of lung volume. Another factor often unappreciated is the effect of tuberculous caseous pneumonia or bronchopneumonia which by decreasing aerated parenchyma and distensibility lowers intrathoracic pressure and exerts traction on the bronchial wall, producing ectasia.

*Pathology.*—The essential process in bronchiectasis has been described as an ulcerative lesion in the bronchi with destruction of the epithelium, muscle and elastic fibers of the bronchi and frequent extension of the destructive process into the surrounding tissues of the lung. This process is furthered by stenosis of the bronchus, a stenosis causing retention of infective secretions and weakening of the elastic tissues, resulting in dilatation of the bronchial walls. Two main types

of bronchiectasis are recognized the saccular and the cylindrical

Bronchiectasis may be unilateral or bilateral and may involve segments of one or more lobes It occurs most frequently in the lower lobes particularly in the left lung Bronchiectasis in the lingula of the left upper lobe often occurs simultaneously with bronchiectasis *in the left lower lobe It occurs* less frequently in the right bronchus since the latter is a more direct continuation of the trachea and drainage is more efficient whereas the left bronchus is not only constricted by the left pulmonary artery but is narrower and comes off the trachea at a more acute angle than does the right lower lobe bronchus

*Incidence* —The incidence of bronchiectasis is difficult to determine Most cases develop in childhood or early adult life

*Clinical Manifestations* —The first symptom is usually a persistent cough Sputum sometimes fetid or foul may be expectorated in amounts varying from a few ounces to 1000 cc daily The sputum is more copious in the morning, owing to retention of secretions during the night The patient may be free from expectoration for the remainder of the day At times the sputum is streaked with blood and at irregular intervals, there may be a severe hemoptysis amounting sometimes to a pint of blood This may cause a suspicion of the presence of tuberculosis or a lung abscess The hemoptysis is rarely followed by any significant aftereffects except that of alarm on the part of the patient or his family It is seldom fatal When the sputum is foul it gives rise to a persistent offensive breath Slight fever may accompany the cough and hemoptysis Clubbing of the fingers often to slight degree *with incurvation of the nails has been ob*served in long standing cases

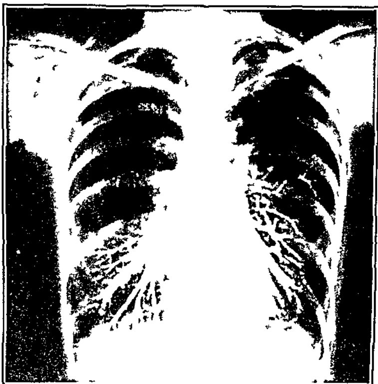


Fig 148 —Bilateral cylindrical bronchiectasis in lower lobes

Except for recurrent attacks of bronchitis and bronchopneumonia which occur mostly in the winter months the patient may have the appearance of general good health for long periods of time after onset of the disease without evident change in respiratory rate significant rise in temperature, or

tachycardia Chest pain is uncommon The disease may be present for years without causing physical deterioration The physical signs are not pathognomonic and are usually those of chronic pneumonitis or fibrosis or those of the associated or complicating disease (bronchopneumonia empyema or lung abscess) Palpation reveals tactile fremitus increased in cases of extensive pulmonary fibrosis or decreased when the pleura is markedly thickened Resonance is the rule on percussion except in the presence of peribronchial infiltration where dullness is noted Hyperresonant to tympanitic notes are elicited if the dilated bronchi are near the surface but dullness is found when the cavities are filled with pus Many types of rales may be heard particularly in advanced cases but not consistently

Examination of the sputum reveals such organisms as are found in bronchitis Those most characteristic are fusiform bacilli spirilla and anaerobic bacilli streptococcus hemolyticus and nonhemolyticus streptococcus viridans staphylococcus albus and aureus pneumococcus and hemophilus influenzae

*Diagnosis* —Diagnostic measures include a careful study of the history of susceptibility to colds pneumonitis or tuberculosis and the possibility of the presence of a foreign body supplemented by a physical examination and laboratory bronchoscopic and *x* ray studies

Routine roentgenologic examination gives little information In severe cases it may show a depressed diaphragm peribronchial fibrosis and irregular fibrotic mottling Cyst like shadows in the apical area of the upper lobe may represent emphysematous blebs while some may indicate bronchiectatic dilatations often resulting from tuberculous processes The appearance of large multiple cysts are suggestive of congenital bronchiectasis It must be remembered that a normal roentgenogram does not indicate the absence of bronchiectasis

Bronchography affords the only sure evidence of bronchiectasis and consists of instillation of iodized oil into the bronchial tree after thorough postural drainage By outlining in turn the bronchioles of each lobe the type and extent of the disease can be determined Involved segments reveal bronchiolar dilatation of a cylindrical (tubular) or saccular (grape like cluster) type the extent of involvement being a guiding factor in the selection of cases for surgery

Bronchoscopic inspection may reveal the presence of foreign bodies or other obstruction It is valuable in investigating ectasia produced by bronchial lesions in revealing the character of the exudate and in detecting bronchial orifices from which the exudate originates

*Prophylaxis* —It is now possible in large measure to prevent bronchiectasis Early diagnosis and proper care of measles whooping cough and bronchopneumonia will prevent many cases of the disease Control of sinus infection prompt removal of foreign bodies endothoracic new growths and bronchial strictures (where possible) will do much to prevent interference with bronchial drainage and dilatation of the bronchi

*Medical Treatment* —Treatment of bronchiectasis is both medical and surgical Since the anatomical changes produced by bronchiectasis are irreversible the medical therapy must be chiefly symptomatic Medical measures must be directed not only toward relief of symptoms but toward removal of etiologic factors

Symptoms in some instances can be relieved by proper medication and postural drainage Postural drainage is widely advocated since this procedure produces a maximal evacuation of secretion Patients are advised to lean over the edge of the bed to allow the exudate to accumulate in the bronchi and gravitate to the trachea from which is is easily expectorated This should be done three times daily Adequate postural drainage in some cases brings such dramatic relief that patients are able to continue their activities for years without great discomfort Hanging from the hips over the side of the bed with the head almost touching the floor or bending over a stool in a like manner for fifteen minutes will usually loosen the secretions so that they can be expectorated on assuming a sitting position Postural drainage is most helpful when performed just before retiring and again on rising in the morning Expectorants help to decrease the viscosity of the secretions

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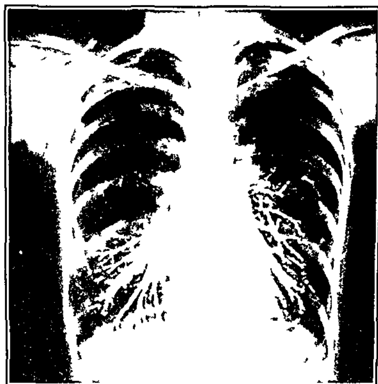


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The course of bronchiectasis without surgical therapy is steadily downward with possible development of such complications as heart failure, brain and lung abscesses, empyema, amyloidosis, pneumonitis, pneumothorax and pulmonary fibrosis with emphysema.

If bronchiectasis is initiated in early adulthood and is not treated surgically, life expectancy beyond middle age can hardly be hoped for.

After surgical intervention, the mortality rate is low and prognosis for complete recovery is good. This is particularly true now that the use of the antibiotics has become common both before and after operation.

## Bronchial Stenosis and Obstruction

*Definition.*—Bronchial obstruction is mechanical interference with normal ventilation and drainage of the lung. Bronchial stenosis is narrowing of the lumen of the bronchi.

*Pathologic Physiology.*—The intrathoracic pressure during quiet breathing in the healthy individual is sub-atmospheric during both phases of the respiratory cycle except during coughing or straining. However, in the presence of obstruction to the free flow of air into and out of the lungs, strong inspiratory and forced expiratory efforts, or coughing and muscular straining, the intrathoracic and intrapulmonary pressure may be increased ten times. Normally the lumen of the bronchus widens during inspiration and narrows during expiration. When the air intake is increased by respiratory demands and expiration is interfered with, as in cases of stenosis, an increasing amount of air is trapped in the lung. Respiratory balance is restored only if the intrapulmonary air behind the occlusion overcomes the resistance to expiration. Normal bronchi are directly related to ventilation and drainage of the lung, to intrapulmonary pressure and to circulatory balance.

Cough, the function of which is removal of secretions and obstructions, produces maximum reduction of the bronchial diameter and so prevents air from escaping. This reduction of the bronchial diameter during cough is irregular, the walls of the bronchi not remaining parallel, so that stenosis may progress to complete obstruction. Complete stenosis usually results in atelectasis.

*Etiology.*—Bronchial stenosis may be congenital or acquired. When *congenital*, pressure on the bronchi during fetal development may have brought about a deformity of the whole lung and of the larger bronchi and their alveoli, so that the lung becomes a vast unilocular or multilocular cyst. An anomaly developed later in fetal life may affect only a few smaller bronchi and cause only small intrapulmonary cysts. Such cysts may lie against the wall of a large bronchus and compress its lumen. But this is rare.

*Acquired bronchial stenosis* may be *extrabronchial* (as a result of pressure on or invasion of the lumen by a pathologic process in adjoining areas) or *endobronchial* (as a result of intrinsic disease of the air passages) or *intrabronchial* (as a result of occlusion by foreign bodies). The stenosis is brought about by swelling of the mucosa, by obstructive exudates which accumulate when cough is ineffective, or by outward or inward increase in pressure so that partial or complete obstruction ensues.

*Intrabronchial* stenosis may be caused by foreign bodies, plugs of adhesive exudates, inflammatory lesions or tumors.

Bronchial stenosis frequently develops after severe or chronic infections of the tracheobronchial tree, such as measles, whooping cough, pneumonia, influenza, scarlet fever and asthmatic bronchitis.

Tumors usually occur in only one lobe. Tuberculous granulations and non-tuberculous inflammatory constrictures usually develop in only one of the large bronchi.

Stenosis of the middle bronchi is generally caused by the presence of small foreign bodies or by diffuse sclerosing processes such as pneumoconiosis and tuberculosis. Blockage of these smaller bronchi causes the alveoli to be blown out into emphysematous blebs. On the other hand, constriction of the bronchioles and obstruction of their lumen by swelling of the mucosa may follow bronchitis and influenzal infections or inhalation of fumes, smoke or gases.

*Symptoms and Signs.*—Symptoms in the early stages of bronchial stenosis may be lacking except for slight discomfort on exer-

while postural drainage is being carried out This procedure is the best method of treatment when the sputum is foul and annoying to the patient

Repeated bronchoscopic aspirations of sticky secretions are sometimes found valuable in advanced cases in which postural drainage has proved inadequate Such aspiration may bring relief for weeks if followed by postural drainage

Bed rest is advisable in the presence of fever and distressing cough The diet should be adequate and have a high protein a high caloric and a high *vitamin content*

Antimicrobial drugs although of no permanent effect on bronchiectasis are of great value in treating acute episodes of respiratory-tract infections and in improving the general condition of the debilitated bronchiectatic patient Cough and the amount of retained exudates are reduced the temperature is lowered and given postoperatively, the antibiotics may prevent such complications as emphysema atelectatic pneumonia, *and hematogenous dissemination of the in*fection

*Surgical Therapy* —Only resection of the affected pulmonary tissues can bring certain and permanent cure Internist and surgeon should work together, for physicians who routinely advise against surgical interference in bronchiectatic patients are assuming a great responsibility Since bronchiectasis is an irreversible process it must always be borne in mind that medical measures such *as postural drainage* and use of the antimicrobial drugs are primarily palliative only Except in patients with minimal disease only complete removal of the involved area is permanently effective Unfortunately many patients are seen when the bronchiectasis has become so extensive that neither lobectomy nor pneumonectomy will be effective

The age of the patient and particularly the extent of the disease determine whether the operation should be *performed* Pulmonary resection is highly successful in children, who have a more rapid and more nearly complete recovery than older patients Postoperative morbidity and mortality increase with the age of the patient

Patients in poor general health must first be brought into good condition and concurrent diseases must be brought *under control* before operation is attempted Aerosol therapy is advocated for one week before the operation or until the sputum is reduced to minimum and for an indefinite period after the operation Bronchoscopic aspiration immediately preceding operation is recommended

Bilateral bronchiectasis is often a contraindication for operation but a number of patients have had bilateral operations that *have proved successful In bilateral bron*chiectasis, only one lobe is removed in the first stage later when compensatory adjustments have been made the lobe on the other side may be removed The operation, being elective is preferably performed after the winter and early spring months, during which respiratory infections are most common

Lobectomy is the method of choice in treatment of most types of bronchiectasis *Lobectomy and partial or total pneumonec*tomy now have a death rate of only about 3 per cent

Bilateral lobectomy has a high mortality rate since the patient is subjected to two operations and while convalescing from the first operation is liable to secondary infection from the remaining bronchiectatic infection Souders noted that when about 70 per cent of the disease is in one lung removal of the diseased portion of that lung *may result in such improvement that* resection of the remaining diseased areas may not be necessary If found necessary the second operation can be performed later Usually bilateral surgery is performed in two stages six months to one year elapsing between operations

*Prognosis* —The prognosis is poor in non treated or unsuccessfully treated cases of bronchiectasis The patient may contract the disease early in life yet live to old age but in all the years between he may be extremely uncomfortable and unhappy perhaps totally disabled Protracted invalidism economic insecurity and a lonely hopeless life may lead to a psychopathic personality and prove a greater problem to the physician than the disease itself

*Pathologic Physiology.*—When a non-opaque body lodges in the bronchus severe edema of the bronchial mucosa follows increasing the bronchial obstruction. Since the bronchi widen on inspiration only partial obstruction may be caused by the foreign body and sufficient space remains between it and the bronchial wall to allow entrance of air (ball valve mechanism) but on expiration with narrowing of the bronchus the edema more or less prevents escape of the air from the lung. This in turn leads to retention of excess air in the segment immediately distal to the bronchus a condition eventually leading to emphysema. This is called the expiratory check valve mechanism which becomes complete as irritation leads to plugging of the bronchus (stop-valve mechanism). When the foreign body has thus finally completely blocked the bronchus the air below the foreign body is slowly absorbed atelectasis follows. The stop-valve mechanism may develop rapidly within a few hours especially when the foreign body is vegetable matter (like a bean) and swells rapidly. Occasionally the foreign body causes a chemical action as well producing further irritation of the tissues sometimes the action is biochemical or allergic.

*Signs and Symptoms.*—With distension of the lung the percussion note becomes hyperresonant or tympanitic voice sounds are absent and breath sounds are heard only when some inspired air has penetrated the blocked-off segment of the lung before distention is complete. Pneumothorax may be suspected. Seldom however does the contained air burst through a weakened portion of the lung surface to create a pneumothorax. Roentgen examination reveals transparency of the affected side because of its excess air content. The heart and mediastinum are displaced toward the normal side by the distended lung this depresses the diaphragm on the affected side and restricts its movements. Movement on the sound side is therefore increased and at the end of expiration this contrast in the transparency of the two lungs is quite evident. This is not noted during inspiration.

The symptoms depend on the size and nature of the foreign body. The bronchial lumen because of irritation and inflammation of the mucous membrane may be obstructed and in turn cause an intense inflammatory reaction. The position of the foreign body and the retained exudate together with emphysema and atelectasis and the occasional shifting of the object all tend to influence the general clinical picture. The lower down the foreign body goes in the respiratory tract the less the irritation and discomfort. If it is in the larger bronchi and moving up and down with respiration irritation of the mucous membrane of the trachea will produce a cough. Yet as the object comes to rest the patient may be unaware of its continued presence for an extended period or until secondary symptoms arise. It may be weeks or months before complete blockage takes place.

In addition to cough there may be dyspnea and pain. Fever usually develops later. Wheezing is heard in most cases. A symptomless period may be followed by severe cough blood streaked sputum a metallic taste and a specific odor depending on the nature of the foreign body. Vegetable matter may cause laryngotracheal bronchitis attended by irregular fever. When symptoms develop the roentgenogram may suggest the presence of an unresolved pneumonia an obvious atelectasis bronchiectasis abscess or empyema may be diagnosed but the true cause is often unsuspected.

Prognosis is good if spontaneous expulsion of the foreign body occurs but this is rare. Recovery is generally assured if removal of the foreign body is prompt. The younger the patient the more dangerous is the condition particularly if the object is of vegetable matter since such material may cause suppuration.

*Treatment.*—The only cure possible is removal of the foreign body by means of bronchoscope. This requires skilled operators. Inverting the patient and shaking him an old family remedy is dangerous since the object may lodge in the glottis and cause suffocation.

## REFERENCES

***Bronchitis Bronchiectasis Bronchial Stenosis***


ADAMS R and FICARRO B J Appraisal of Surgery in Treatment of Bronchiectasis J A M A 1947 *134* 240

tion Wheeze, dyspnea, and cough are the most common symptoms Wheeze is noted invariably in progressive bronchial obstruction Jackson observes that the patient with one lung entirely atelectic may be short of breath only on exertion if the other lung is correctly functioning Obstructive emphysema causes dyspnea only when both lungs are affected When only one major bronchus is involved the dyspnea is not severe and the patient is uncomfortable only on exertion Breathlessness is very apparent on exertion in high stenosis of the trachea or both bronchi at the bifurcation but disappears when the patient is lying down

Stridor, which is loud in stenosis of the trachea and sometimes in stenosis at the bifurcation is absent in diffuse stenosis of the small bronchi a point of differentiation according to Floesser

Stenosis of the larger bronchi is characterized by a loud brassy nonproductive cough of mediastinal or tracheal irritation When cough is productive the sputum is copious watery and frothy, if the obstruction is sufficiently severe to cause distal atelectasis If the sputum is blood streaked the phenomenon is due to the underlying process Abundant thin purulent sputum may alternate with a dry unproductive cough and indicate an intermittent stenosis Foul and purulent sputum is indicative of an infective process

*The clinical finding of a localized wheeze is* suggestive of bronchial stenosis especially when heard at the end of a forced expiration

The degree of resonance and dullness vary with the extent of complicating obstructive emphysema and atelectasis Atelectasis should be suspected when findings indicate displacement of the trachea heart mediastinum and chest wall

*Diagnosis* —The diagnosis of bronchial obstruction should be suggested when the characteristic signs and symptoms are observed and confirmed by fluoroscopic radiographic and bronchoscopic examinations Roentgenograms may demonstrate the presence and site of the obstruction and indicate the condition of the adjacent pulmonary tissues but they cannot show the cause of the stenosis Bronchoscopy is necessary in every suspected case of broncho stenosis It frequently reveals the site, degree, and extent of the obstruction and often demonstrates extrabronchial pressure and the presence of intrabronchial tumors ulceration, and scars

Bronchography is not advisable where possible aggravation of the occlusion might result Laminagrams are valuable in demonstrating narrowing of a bronchus

*Treatment* —Definitive treatment depends on the cause of the obstruction Peroral aspiration of the tracheobronchial tree with restoration of normal drainage by ciliary motion tussive squeeze, and bechic blast—this is the only method of obtaining relief of bronchial obstruction and, for this, bronchoscopic aspiration is necessary The bronchoscope is also used to study the bronchial conditions following aspiration of accumulations Jackson finds that direct laryngoscopic and bronchoscopic aspiration will, with ample power supplied by the negative pressure pump remove even semisolid exudates

Medical care is essential in most cases to restore normal drainage Usually patients are so relieved after bronchoscopic aspiration that they immediately enjoy normal activities Such patients however require a strictly enforced regime of medical care and management, with rest in bed for from 12 to 18 hours daily a well balanced diet taken in three meals a day vitamin therapy, *and in allergic patients desensitization* Autogenous vaccines and antibiotics may be helpful Opiates sedatives and expectorants should be avoided

## Foreign Bodies in the Bronchi

The lodging of foreign bodies in the air and food passages is very common Ninety per cent of the cases of foreign bodies lodged in the bronchi are said to occur in children under two years of age One of the principal reasons for this is children s carelessness in putting objects in the mouth haste in eating and swallowing and playing while eating and drinking The symptoms may be long delayed or may be only slightly annoying for many years Metal objects are often tolerated without symptoms for they usually become covered with a calcareous concretion

### Ventilation and Ventilatory Insufficiency

Ventilation can be considered a mechanical phenomenon because air flow in the lungs is the result of variations in pressure in the alveoli and tracheobronchial tree induced by periodic movements of an air pump consisting of the chest wall diaphragm and other muscular structures The range of variation of alveolar pressure during the respiratory cycle is quite small normally from a few mm Hg below to a few mm Hg above atmospheric pressure It is commonly accepted that stresses exerted by this air pump produce variations in intrapleural pressure also which are of greater amplitude than those occurring in the alveoli One must emphasize however, that the microscopic film of fluid present in the pleural space creates cohesive forces between the two sheets of pleura which prevent their separation and that under normal conditions no intrapleural pressure can be measured during the respiratory cycle Pleural pressure variations can be measured only after introduction of air and creation of an intrapleural space Under these conditions the pleural pressure is a reflection of the balance of opposing forces created by (*a*) the moving chest bellows and (*b*) the elastic lung

During inspiration the lungs enlarge as shown by Keith according to a definite pattern which is determined by the actual structure of the lungs on the one hand and the movements of the chest bellows on the other The great fissure is of functional significance in this regard The two upper lobes together with the middle lobe on the right are expanded by the action of the muscular and bony structures of the neck and shoulder girdle the first five ribs and the upper two-thirds of the sternum This section of the chest moves upward and forward on inspiration expanding the underlying lung in exactly the same manner Expansion of the two lower lobes is quite different being dependent upon the action of the diaphragm and of the lower ribs excepting the 11th and 12th which are a part of the abdominal wall When the intercostal muscles attached to these ribs contract on inspiration there occurs in addition to a forward movement of the lower sternum considerable lateral displacement of the lower chest The diaphragm acts much like a piston moving downward and forward on contraction displacing the abdominal contents before it As a result of these motions the lower lobes are expanded laterally forward and downward Their apical regions being relatively fixed this expansion is accomplished with considerable sliding of the visceral over the parietal pleura The musculature of the abdominal wall itself also plays an active although not always obvious part in respiration by relaxing during inspiration and contracting during expiration and thus must be considered a part of the chest bellows This is most apparent during forced expiration when strong contraction of the abdominal musculature occurs

Normal ventilation necessitates expenditure of energy on the part of these various muscles of respiration in order that certain resistive forces be overcome These forces include the elasticity of the lungs and chest wall the viscous and turbulent resistance of air movement in the respiratory passages and the resistance to deformation always present in living tissue a property that must be differentiated from elasticity Kinetic energy imparted to the air is probably of negligible importance as is the energy involved in acceleration and deceleration of the entire system even though during maximum breathing efforts peak rates of air flow have been shown to reach as much as 400 liters per minute The resistive forces are normally quite small in comparison to the motive powers of the muscles of respiration In terms of air flow this is manifest in the fact that the chest bellows is ordinarily capable of providing an amount of ventilation far greater than anything required by bodily activity This means that under normal conditions there is always an excess of ventilatory capacity over the ventilation required The excess ventilatory capacity when expressed as the difference between observed ventilation and the measured maximum voluntary or reflex breathing capacity is known as the *breathing reserve* This is of considerable importance in any consideration of pulmonary function because in nor-

ALEXANDER JOHN Rôle of Medicine and Surgery in Management of Bronchiectasis Ann Int Med 1944 *21* 565
ANSPACH P M Atelectasis and Bronchiectasis in Children A Study of Fifty Cases Presenting a Triangular Shadow at the Base of the Lung Am J Dis Child 1934, *47* 1011
BEST C H and TAYLOR N B Physiological Basis of Medical Practice Baltimore Williams & Wilkins Co 5th ed 1950
CAMPBELL D C Bronchiectasis Univ Minn Thesis 1941
CARDON LEONARD *et al* Acute Suppurative Bronchitis and Bronchiolitis in Chronic Pulmonary Disease Ann Int Med 1951 *34* 559
DIACK S L Clinical Aspects of Bronchiectasis Portland Clin Bull 1948 *1* 67
DI RIENZO S Functional Bronchial Stenosis Surgery 1950 *27* 853
EASTLAKE C JR Aerosol Therapy in Sinusitis Bronchiectasis and Lung Abscess Bull New York Acad Med 1950 *26* 423
ELOESSER L Bronchial Stenosis J Thoracic Surg 1931 *1* 194
FREEDMAN F and BILLINGS J H Active Bronchopulmonary Lithiasis Radiology 1949 *53* 203
FRIEDMAN L L and CARTER S B Chronic Bronchitis and Bronchiectasis In KYSER F A Therapeutics in Internal Medicine New York Nelson 1950
HEDBLOM C A Pathogenesis of Bronchiectasis Surg Gynec and Obst 1931 *52* 406
HOLMES C H Chronic Bronchitis Dis Chest 1940 *6* 199
JACKSON C and JACKSON C L Bronchoesophagology Philadelphia W B Saunders Company 1950
KAY E B MEADE R H JR and HUGHES F A JR Surgical Treatment of Bronchiectasis Ann Int Med 1947 *26* 1
KERGIN F G Surgical Treatment of Bilateral Bronchiectasis J Thoracic Surg 1950 *19* 257
KINNEY W M Bronchiectasis A Neglected Disease Dis Chest 1947 *13* 33
LISA J R and ROSENBLATT M B Bronchiectasis New York Oxford University Press 1943
LISTER W A Chronic Bronchitis Never a Complete Diagnosis Lancet 1949 *1* 719
LYONS H A Diagnosis of Bronchial Stenosis Dis Chest 1950 *18* 16
MILLER J A Pathogenesis of Bronchiectasis J Thoracic Surg 1934 *3* 246
MYERS J A and MCKINLAY C A Chest and Heart Springfield Charles C Thomas v 1 1948
OGILVIE A G Natural History of Bronchiectasis Arch Int Med 1941 *68* 395
RIGGINS H M Bronchiectasis Morbidity and Mortality of Medically Treated Patients Am J Surg 1941 *54* 50
ROPER F A Chronic Bronchitis in the Elderly Practitioner 1942 *148* 18
SCHMIDT H W Benign Nontuberculous Bronchial Stenosis Arch Otolaryng 1944 *39* 43
SCHMIDT H W CLAGETT O T and MCDONALD J R Broncholithiasis J Thoracic Surg 1950 *19* 226
SINGER J J Differential Diagnosis of Chest Diseases Philadelphia Lea & Febiger 1949
SOKOLOFF M J Bronchiectasis M Clin North America 1947 *31*, 1418
SOLDERS C I Bronchiectasis and Its Management Report of 277 Cases Dis Chest 1949 *16* 381
SOUTHWELL N Chronic Bronchitis Brit J Indust Med 1946 *3* 75
STEEL, R S Bronchitis Especially Chronic M J Australia 1944 *2* 273
THILBERG N F Penicillin Instillation in Bronchiectasis South M J 1948 *41* 873
WEST J C Surgical Considerations in Bronchiectasis Surg Clin North America 1950 *30* 1299

# PULMONARY FUNCTION IN SUB-ACUTE AND CHRONIC DISEASES OF THE LUNGS

BY ANDRE COURNAND M D AND JOHN R WEST M D

## PRIMARY FUNCTION OF THE LUNGS

An appreciation of the clinical manifestations of subacute and chronic diseases of the lungs necessitates first an understanding of the various factors involved in pulmonary function and second an awareness of the means by which these factors may be altered by disease

Aeration of the blood the primary function of the lungs is a complicated process having three major components These are (1) pulmonary ventilation or the mass movement of air into and out of the lungs (2) the exchange of oxygen and carbon dioxide between this air and the blood and (3) the mechanisms by which ventilation is regulated so as to provide the amount of respiratory gas exchange demanded by the metabolic needs of the body That these components are closely interrelated is apparent Nevertheless this division is a useful one for purposes of discussion and will be adhered to in the following brief outline of pulmonary function and dysfunction

this, regional blood flow in the lungs is readily influenced by local mechanical factors. Consequently narrowing or obliteration of smaller vascular channels as well as local variations in pulmonary elasticity induced by pathologic change may greatly alter the distribution of capillary blood to the alveoli. Furthermore in pulmonary disease in which large and small air ways are variably obstructed uneven distribution of inhaled air may become marked and may lead to hypoventilation of certain areas with considerable reduction in oxygen tension and elevation of carbon dioxide tension in the alveoli concerned. When these disturbances in the distribution of air and blood in the lungs affect significant numbers of alveoli defective gas exchange results.

Whenever ventilation is maintained but perfusion of alveoli is reduced or obliterated gas exchange across the membrane is reduced or eliminated. Physiologically, ventilation of such alveoli is indistinguishable from ventilation of the tracheobronchial tree (the anatomic dead space) hence the presence of large numbers of these alveoli results in increased *dead space like ventilation*. Excessive dead space ventilation throws a greater than normal burden in respect to gas exchange upon remaining normal alveoli and adequate carbon dioxide elimination can take place only when the normally perfused alveoli are hyperventilated (Fig 149). An adequate oxygen intake however with only slight reduction in arterial oxygen saturation can occur *without* hyperventilation in most instances of excessive dead space ventilation because of the special affinity of blood for oxygen in the range of alveolar oxygen partial pressures which would be found.

Conversely whenever alveolar ventilation is reduced while perfusion is maintained at a normal level the blood does not become fully arterialized in the capillaries. The effect upon arterial blood of mixing this fraction of capillary blood (partially oxygenated) with the remainder (fully oxygenated) is similar to that of a true veno arterial shunt the magnitude of which may be estimated. This virtual shunt together with actual right to left shunts passing through bronchial and thebesian veins has been termed *venous admixture*. Venous admixture results in arterial anoxia as well as a *tendency* towards carbon dioxide retention. The latter may not be realized if sufficient hyperventilation of remaining well ventilated, perfused alveoli occurs. Arterial anoxia due to venous admixture cannot however be corrected to any significant degree by hyperventilation of normal alveoli (Fig 149).

The physical properties of the alveolo capillary membrane its total area in the lungs and the partial pressure differences on either side of the membrane determine the rates at which respiratory gases diffuse between alveolar air and blood. The membrane is vastly more permeable with respect to carbon dioxide than it is with respect to oxygen a reflection of the difference in solubility of the two gases in watery solutions but even so the normal membrane never offers a significant barrier to oxygen transfer. If the membrane is altered by disease however it may inhibit the diffusion of oxygen to a variable extent. Even in the presence of considerable disease this impairment will result in significant arterial anoxia only under conditions in which there is a large amount of oxygen to be transferred per unit time as for example during physical exercise or under conditions wherein the inspired air has a low oxygen concentration as in residence at high altitudes. In some rare instances of severe non homogeneous alterations of the alveolo-capillary membrane throughout the lung oxygen diffusion may become so impaired in some areas that transport of this gas ceases entirely under physiologic conditions and transport of carbon dioxide becomes impeded. Ventilation of alveoli involved in such a process contributes to dead space ventilation and perfusion to venous admixture. Consequently in these instances arterial anoxia may be present at rest and carbon dioxide retention may occur.

From these considerations it is apparent that impaired gas exchange in pulmonary disease can be attributed to one or more mechanisms (1) ventilation of poorly perfused areas—dead space like ventilation (2) perfusion of poorly ventilated areas—venous admixture and (3) impaired diffusion of oxygen across the alveolar capillary membrane—reduction in oxygen diffusing capac-

mal individuals and in most patients with pulmonary disease there appears to be a definite correlation between the size of the breathing reserve and the consciousness of difficult breathing *i e* dyspnea Obviously, the breathing reserve can be reduced in either of two ways *i e* increasing the breathing requirement or decreasing the breathing capacity or by both No matter what the cause or what the mechanism whenever breathing reserve is reduced to such an extent that dyspnea ensues *ventilatory insufficiency* can be said to be present For example bronchospasm and bronchiolar obstruction found in asthma and pulmonary emphysema increase the viscous and turbulent resistance to air movement in the smaller respiratory passages and, therefore lead to great reduction in ventilatory capacity In consequence breathing reserve may by slight exercise be reduced below the level at which dyspnea appears In some of these patients ventilatory capacity may become so impaired that dyspnea is present at rest Conversely other pulmonary diseases to be discussed in more detail later are characterized by reduction in breathing reserve as a result of the increase in ventilatory requirement they engender Although the mechanism is distinctly different the result is the same *viz* a decrease in the breathing reserve and production of dyspnea

It must be mentioned that the rhythmic action of the chest bellows affects pulmonary blood flow (and therefore cardiac output) as well as air flow During inspiration the amount of blood flowing into the lungs increases, while the outflow diminishes In expiration the reverse process occurs *i e* inflow decreases while left heart output is augmented

## Gas Exchange and Alveolar Respiratory Insufficiency

Respiratory gas exchange is a physicochemical process which depends upon differences in partial pressure of oxygen and carbon dioxide on either side of the structures separating air and blood in the lung *i e*, the alveolo-capillary membrane as well as the physical properties and the area of this membrane

Because the amount of air taken into the lungs in a single breath during quiet breathing (resting tidal volume) is quite small in relation to the amount of air remaining in the lungs at the end of a quiet expiration the composition of alveolar air remains fairly constant throughout the respiratory cycle At sea level the normal values approximately, for the partial pressure of the respective gases present are carbon dioxide 39 mm Hg, oxygen 103 mm Hg, water vapor 47 mm Hg nitrogen and other inert gases 571 mm Hg In mixed venous blood entering the pulmonary capillary the partial pressure of oxygen is considerably lower and that of carbon dioxide slightly higher than these values, being approximately 35 and 45 mm Hg respectively These pressure differences bring about gas exchange *i e*, diffusion of carbon dioxide from blood into alveolar air and diffusion of oxygen from alveolar air into blood Capillary blood leaving the alveoli is as a result of this exchange in nearly perfect gaseous equilibrium with alveolar air in respect to carbon dioxide oxygen, and nitrogen under normal circumstances Inasmuch as the partial pressure of nitrogen in the blood is not affected by gas exchange it is apparent that the total gas pressure in the venous blood is considerably less than atmospheric pressure

The concentrations of the respiratory gases in alveolar air and capillary blood are dependent in large part upon the efficiency of alveolar ventilation on the one hand and the adequacy of alveolar perfusion with blood on the other In the normal lung neither inhaled air or mixed venous blood is *uniformly* distributed to all functioning alveoli but the degree to which distribution is impaired is slight and therefore relatively few alveoli are well perfused but poorly ventilated or poorly perfused but well ventilated This normal relationship between alveolar ventilation and perfusion is however subject to considerable alteration by disease In this respect emphasis must be placed upon the most distinctive characteristic of the pulmonary circulation namely that it is a low pressure system Because of

this, regional blood flow in the lungs is readily influenced by local mechanical factors. Consequently, narrowing or obliteration of smaller vascular channels as well as local variations in pulmonary elasticity induced by pathologic change may greatly alter the distribution of capillary blood to the alveoli. Furthermore, in pulmonary disease in which large and small air ways are variably obstructed, uneven distribution of inhaled air may become marked and may lead to hypoventilation of certain areas with considerable reduction in oxygen tension and elevation of carbon dioxide tension in the alveoli concerned. When these disturbances in the distribution of air and blood in the lungs affect significant numbers of alveoli, defective gas exchange results.

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Because the amount of air taken into the lungs in a single breath during quiet breathing (resting tidal volume) is quite small in relation to the amount of air remaining in the lungs at the end of a quiet expiration, the composition of alveolar air remains fairly constant throughout the respiratory cycle. At sea level the normal values approximately, for the partial pressure of the respective gases present are: carbon dioxide 39 mm Hg, oxygen 103 mm Hg, water vapor 47 mm Hg, nitrogen and other inert gases 571 mm Hg. In mixed venous blood entering the pulmonary capillary the partial pressure of oxygen is considerably lower and that of carbon dioxide slightly higher than these values, being approximately 35 and 45 mm Hg respectively. These pressure differences bring about gas exchange, *i e* diffusion of carbon dioxide from blood into alveolar air and diffusion of oxygen from alveolar air into blood. Capillary blood leaving the alveoli is, as a result of this exchange, in nearly perfect gaseous equilibrium with alveolar air in respect to carbon dioxide, oxygen and nitrogen under normal circumstances. Inasmuch as the partial pressure of nitrogen in the blood is not affected by gas exchange it is apparent that the total gas pressure in the venous blood is considerably less than atmospheric pressure.

The concentrations of the respiratory gases in alveolar air and capillary blood are dependent in large part upon the efficiency of alveolar ventilation on the one hand and the adequacy of alveolar perfusion with blood on the other. In the normal lung neither inhaled air or mixed venous blood is *uniformly* distributed to all functioning alveoli, but the degree to which distribution is impaired is slight and therefore relatively few alveoli are well perfused but poorly ventilated or poorly perfused but well ventilated. This normal relationship between alveolar ventilation and perfusion is, however, subject to considerable alteration by disease. In this respect emphasis must be placed upon the most distinctive characteristic of the pulmonary circulation, namely that it is a low pressure system. Because of

This concept is useful also in interpreting changes in ventilation that have been observed in a variety of pulmonary disorders. For example, in certain diseases characterized by a reduction in the oxygen diffusing capacity of the lungs, acute arterial anoxia occurs on exercise and is associated with hyperventilation which is probably due to increased chemoreflex drive. In many of these patients, however, hyperventilation is observed at rest when no arterial anoxia is present. In the majority of such cases the level of blood bicarbonate is reduced (probably a result of repeated bouts of hyperventilation caused by increased physical activity) and the medullary center can therefore be presumed to be *supranormally* sensitive to the carbon dioxide stimulus. Conversely, in certain cases of pulmonary emphysema with arterial anoxia and chronic carbon dioxide retention, ventilation seems to be chiefly controlled by the chemoreflex drive induced by the anoxia because, as a result of an increased blood bicarbonate level, the medullary center has become *infranormally* sensitive to the carbon dioxide stimulus. The reduction in centrogenic drive is most apparent in these cases when the hypoxic stimulus is removed during oxygen therapy or when carbon dioxide tension is artificially elevated in the inhaled air.

## COMMON PATTERNS OF PULMONARY DYSFUNCTION

### Ventilatory Insufficiency

As stated previously, whenever breathing reserve is reduced to such an extent that excessive dyspnea results from ordinary activity, ventilatory insufficiency is present. This is seen in relatively pure form in several conditions, *e.g.*, (1) mild silicosis not complicated by bronchial obstruction or emphysema, (2) discrete nodular fibrosis of other etiologies, (3) radiation fibrosis, (4) benign forms of pulmonary Boeck's sarcoid and (5) other pleuritic and thoracic processes of varying etiologies. Patients with these disorders complain chiefly of exertional dyspnea which is generally mild to moderate and their only important functional characteristic is an abnormal reduction in breathing reserve during exercise. In some cases this reduction is due to excessive ventilation, in others to reduction in ventilatory capacity, but in the majority to a combination of the two factors. Hyperventilation may be present at rest but this is not marked as a rule. Arterial anoxia is not observed nor is carbon dioxide retention; in fact, it is usual to find a mild compensated respiratory alkalosis. The cause of the resting hyperventilation observed in such cases has been attributed to reflex stimulation arising in the lungs and the osteomuscular frame of the chest induced by the pathologic changes. An additional factor, in all probability, is the effect of the commonly found reduction in blood bicarbonate upon the sensitivity of the medullary center to the carbon dioxide stimulus.

### Alveolo-respiratory Insufficiency

(*a*) *Excessive Dead Space Ventilation.*—In isolated form increased dead space ventilation is observed mostly as a result of large pulmonary air cysts which communicate freely with the tracheobronchial tree. It may follow also repeated embolization of the small pulmonary blood vessels as seen in drug addicts. A similar situation will obtain after accidental ligation of a main branch of the pulmonary artery during surgery. In such an instance ventilation will be maintained with practically no gas exchange occurring in the affected lung.

As has been mentioned previously, a large dead space ventilation necessitates hyperventilation of remaining well perfused alveoli in order to maintain adequate carbon dioxide elimination and normal arterial pCO. The hyperventilation observed in such cases is doubtless due to increased centrogenic drive. Symptomatically, excessive dead space ventilation results in dyspnea and this only if the hyperventilation is extreme because ventilatory capacity remains normal as a rule.

(*b*) *Excessive Venous Admixture.*—This is never observed in pure form as a result of chronic pulmonary disease except in the case of pulmonary arteriovenous fistula. In such cases arterial anoxia, resultant cyanosis and secondary polycythemia may be quite severe. Carbon dioxide retention does not

ity Recently developed techniques have made it possible to quantitate these disturbances as they occur in a variety of pulmonary diseases In so doing the essential physio pathologic disturbances in these disorders have been more closely defined and results of treatment can be assayed

### Regulation of Ventilation

Pulmonary ventilation in the normal individual is under two distinct types of control Pitts has classified these as (1) Chemical—which are concerned with the metabolic and homeostatic demands of the body and (2) Nervous—which are concerned with modification of the basic breathing pattern so as to meet the needs of the moment 'Nervous controls include both cortical and hypothalamic influences as well as certain reflex mechanisms the Hering Breuer reflex pressoreceptor reflexes from the aortic arch and the carotid sinus, various protective reflexes, and reflexes from muscle and joint receptors Persistent hyperventilation in the absence of disordered gas exchange as has been observed in certain types of pulmonary fibrosis has been attributed to alteration in intrapulmonary stretch reflexes of this general type Otherwise these mechanisms are of little clinical importance in pulmonary disease

' Chemical controls are those arising in medullary respiratory center and the peripheral chemoreceptors in the aortic and carotid bodies The medullary center is normally extremely sensitive to changes in arterial $pCO_2$ or arterial pHs responding to very small increments in the former or decreases in the latter with an increase in the respiratory stimulus which has been termed Centrogenic drive The peripheral chemoreceptors in the aortic and carotid glomi are on the other hand chiefly concerned with the hyperventilation which occurs as a result of a decrease in arterial oxygen partial pressure Reduction in arterial oxygen tension is always associated with an increase in electrical activity in the afferent nerves of these bodies, but it is only below a certain critical threshold (arterial $pO_2$ less than 60 to 50 mm Hg ) that the increased stimulus arising in these bodies becomes significant in the regulation of ventilation This stimulus, which is transmitted *through* the medullary center, has been termed 'Chemoreflex drive ' Normal ventilation seems to be the result of centrogenic drive chiefly, the strength of the stimulus depending upon the concentrations of carbon dioxide or hydrogen ions in the respiratory center Whether the actual stimulus is molecular carbon dioxide the hydrogen ion, or both is a matter of some dispute Studies of the respiratory effects of acute anoxia in animals and acute and chronic anoxia in man demonstrating that the sensitivity of the medullary center to the carbon dioxide stimulus varies inversely with the level of blood bicarbonate tend to support the concept that the level of medullary center activity depends upon the pH changes induced within the center by the carbon dioxide produced there metabolically The pH change at the center per unit carbon dioxide produced will depend obviously upon the buffering capacity of the media concerned which is probably related to that of blood plasma The buffering capacity of blood plasma is reflected in the amount of bicarbonate present

Certain well known phenomena of respiration during ascent to an after residence at high altitudes are readily explained according to this view Thus sudden anoxia induced by ascension brings about an increased chemoreflex drive and hyperventilation ensues Hyperventilation causes a reduction in alveolar $pCO_2$ and results in rapid elimination of this gas from the blood A temporary respiratory alkalosis ensues during which medullary center activity is reduced and chemoreflex drive possibly potentiated The alkalosis is gradually corrected by a reduction in the bicarbonate content of the blood As the blood bicarbonate level falls during acclimatization the medullary center becomes increasingly sensitive to carbon dioxide produced *in situ* for reasons stated above and as a result the centrogenic drive increases in strength and finally supersedes the chemoreflex drive If the subject at this stage is relieved of arterial anoxia hyperventilation will continue for some time as a result of the increased centrogenic drive

This concept is useful also in interpreting changes in ventilation that have been observed in a variety of pulmonary disorders. For example, in certain diseases characterized by a reduction in the oxygen diffusing capacity of the lungs, acute arterial anoxia occurs on exercise and is associated with hyperventilation which is probably due to increased chemoreflex drive. In many of these patients, however, hyperventilation is observed at rest when no arterial anoxia is present. In the majority of such cases the level of blood bicarbonate is reduced (probably a result of repeated bouts of hyperventilation caused by increased physical activity) and the medullary center can therefore be presumed to be *supranormally* sensitive to the carbon dioxide stimulus. Conversely, in certain cases of pulmonary emphysema with arterial anoxia and chronic carbon dioxide retention, ventilation seems to be chiefly controlled by the chemoreflex drive induced by the anoxia because, as a result of an increased blood bicarbonate level, the medullary center has become *infranormally* sensitive to the carbon dioxide stimulus. The reduction in centrogenic drive is most apparent in these cases when the hypoxic stimulus is removed during oxygen therapy or when carbon dioxide tension is artificially elevated in the inhaled air.

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occur as a rule because of compensatory hyperventilation. Excessive venous admixture, however, in association with other forms of alveolo-respiratory insufficiency as well as ventilatory insufficiency, plays an important role in the development of the symptoms, signs and physiologic manifestations in chronic pulmonary emphysema, to be discussed in more detail below.

(c) *Reduction in Oxygen Diffusing Capacity.*—This is observed as the main defect in a variety of diseases, e.g., pulmonary scleroderma, pulmonary granulomata of varying etiologies, and miliary infiltrations of the lungs secondary to metastatic carcinoma and to hematogenous tuberculosis. The pattern of dysfunction resulting from this abnormality is one of hyperventilation in all stages of activity, arterial anoxia on exercise, and dyspnea. That anoxia does not occur at rest until late in the course of the disease is not surprising since a reduction in diffusing capacity for oxygen is quite compatible with full saturation of the arterial blood, provided the quantity of oxygen to be transported across the alveolo-capillary membrane is not large. Ventilatory capacity is maintained at normal levels as a rule; hence the exertional dyspnea of which these patients complain is due to a reduction in breathing reserve induced by hyperventilation. Resting hyperventilation is probably due both to proprioceptive reflex stimuli originating in the lungs and to the increase in the sensitivity of the medullary center to the carbon dioxide stimulus, just as in the cases of pulmonary fibrosis mentioned previously. Hyperventilation during exercise is, however, augmented by the effect of reduced arterial oxygen tension upon chemoreflex drive.

### Combined Ventilatory and Alveolo-respiratory Insufficiency

It is less common in practice to find these more or less "pure" patterns of dysfunction as outlined above than it is to find combined forms. For example, while silicosis results chiefly in ventilatory insufficiency, it is not infrequent to find certain patients without complicating emphysema who exhibit varying degrees of impaired gas exchange. Increased dead space ventilation and increased venous admixture, when they are present, however, are rarely of sufficient magnitude to result in significant arterial anoxia and practically never bring about carbon dioxide retention. Reduction in oxygen diffusing capacity also is seldom of such magnitude as to produce signs or symptoms.

The best illustrations of combined ventilatory and alveolo-respiratory insufficiency is that provided by chronic pulmonary emphysema. The patterns of dysfunction observed in this disease range from simple reduction in ventilatory capacity, with mild dyspnea on exertion as the only symptom, all the way to severe arterial anoxia, carbon dioxide retention, dyspnea at rest, and breakdown of the mechanism regulating ventilation. A detailed account of the patho-physiologic aspects of chronic pulmonary emphysema is beyond the scope of this chapter but certain essential features should be pointed out. Ventilatory insufficiency in emphysema is chiefly the result of decreased ventilatory capacity, the compensatory hyperventilation which is frequently observed being of relatively minor importance. Alveolo-respiratory insufficiency results from increased dead space ventilation and venous admixture as well as decreased oxygen diffusing capacity.

The most important feature of emphysema, however, which sets it apart from the other chronic pumonary diseases, is the great reduction in ventilatory capacity which occurs together with disturbance in gas exchange. Because of this the only physiologic means of combatting the effects of disturbed gas exchange, i.e., compensatory hyperventilation, is often lost to the emphysematous patient when it is needed most. This is illustrated in the development of that stage of the disease characterized by breakdown of the mechanism regulating ventilation. As previously mentioned, in certain emphysematous patients with severe arterial anoxia and high arterial carbon dioxide tension, the major stimulus to ventilation is no longer derived from the medullary center but rather originates in the chemoreceptors of the aortic and carotid bodies under the stimulus of arterial anoxia. This stage of the disease is reached as follows.

When ventilatory capacity is no longer adequate to maintain sufficient compensa-

tory hyperventilation progressive carbon dioxide retention develops and this if sustained, is always associated with an increase in the amount of blood bicarbonate This increase in alkaline reserve leads to a reduction in the sensitivity of the medullary

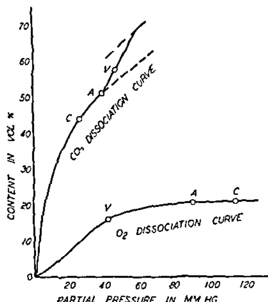



Fig 149 —Representative physiologic dissociation curves of whole blood for carbon dioxide and oxygen drawn to the same scale — — — represents the $CO_2$ curve for fully arterialized blood — — represents the $CO_2$ curve for fully reduced blood V = values for mixed venous blood A = values for mixed arterial blood and C = values for capillary blood derived from hyperventilated alveoli normally perfused

The effects of hyperventilation of normal alveoli upon carbon dioxide excretion and arterial oxygen saturation are apparent from inspection of these curves Reduction in $CO_2$ partial pressure in the blood by hyperventilation results in a significant reduction in $CO_2$ content whereas elevation in $O_2$ partial pressure by hyperventilation will result in only negligible elevation of oxygen content and saturation of the blood

center to the carbon dioxide stimulus a consequent decrease in centrogenic drive to ventilation and more carbon dioxide retention As the vicious cycle thus started progresses centrogenic drive diminishes further and chemoreflex drive increases in importance until finally it becomes dominant When this occurs hyperventilation is usually *no longer observed even if the total* breathing reserve has not been called upon anoxia and gaseous acidosis are intense polycythemia is present as a rule and right heart failure is common The precise reason for the failure of anoxia to induce hyperventilation in these circumstances is not entirely clear Although it might be postulated that prolonged dependency upon the chemoreflex drive which in normal man seems to be a mechanism for temporary activity might result in diminution of its strength this has not yet been shown to be true

*Conclusion* —From this brief introductory discussion it is clear that although the over all function of the lungs can be dissected for purposes of discussion into three main components *viz* ventilation gas exchange and regulation of ventilation these factors are markedly influenced by one another Analysis of pulmonary dysfunction therefore in subacute and chronic pulmonary disease must necessarily be based upon an interpretation of all the factors involved Only in this manner can a clear understanding of the nature of pulmonary dysfunction be reached and rational therapy instituted

REFERENCES


Baldwin E de F Cournand A and Richards D W Jr Pulmonary Insufficiency I Physiological Classification Clinical Methods of Analysis Standard Values in Normal Subjects Medicine 1948 *27* 243

——— Pulmonary Insufficiency II A Study of Thirty nine Cases of Pulmonary Fibrosis Medicine 1949 *28* 1

——— Pulmonary Insufficiency III A Study of 122 Cases of Chronic Pulmonary Emphysema Medicine 1949 *28* 210

Bjurstedt A G H Interaction of Centrogenic and Chemoreflex Control of Breathing During Oxygen Deficiency at Rest Acta Physiol Scandinav 1946 *12* (Suppl 38) 1

Cournand A Cardiopulmonary Function in Chronic Pulmonary Disease The Harvey Lectures 1950–51

Cournand A and Richards D W Jr Pulmonary Insufficiency I Discussion of a Physiological Classification and Presentation of Clinical Tests Am Rev Tuberc 1941 *44* 26

Cournand A Riley R L Austrian R Donald K W and Himmelstein A Studies of Pulmonary Circulation and Gas Exchange in 3 Cases Following the Resolution of Various Diffuse Miliary Infiltrations of the Lungs Trans Assoc Am Phys 1949 *63* 134

Hesser C M Central and Chemoreflex Components in the Respiratory Activity During Acid Base Displacements in the Blood Acta Physiol Scandinav 1949 18 (Suppl 64) 1

KEITH A The Mechanism of Respiration in Man In HILL L ed Further Advances in Physiology New York, Longmans Green and Co London, Edward Arnold, 1909
LILIENTHAL J L JR RILEY, R L PROEMMEL D D and FRANKE R E An Experimental Analysis in Man of the Oxygen Pressure Gradient From Alveolar Air to Arterial Blood During Rest and Exercise at Sea Level and at Altitude Am J Physiol 1947 *147* 199
OTIS A B FENN W O and RAHN H Mechanics of Breathing in Man J Applied Physiol 1950 *2* 592
PITTS R F Regulation of Respiration Chapter 42 in FULTON J F ed A Textbook of Physiology 16th ed Philadelphia W B Saunders Co 1949
RAHN H and OTIS A B Man s Respiratory Response During and After Acclimatization to High Altitude Am J Physiol 1949 *157* 445
RICHARDS D W JR Respiratory System External Respiration In GLASSER O ed Medical Physics Vol 2 Chicago 1950 The Year Book Publishers Inc
RILEY R L and COURNAND A Analysis of Factors Affecting the Concentration of Oxygen and Carbon Dioxide in the Gas and Blood of the Lungs I Theory J Applied Physiol (in press)
RILEY R L DONALD K and COURNAND A Analysis of Factors Affecting the Concentration of Oxygen and Carbon Dioxide in the Gas and Blood of the Lungs II Methods J Applied Physiol (in press)
ROSSIER P H and BLICKENSTORFER L Espace mort et hyperventilation Helvetica Medica Acta 1946 *13* 328
ROSSIER P H and WIESINGER K L insuffisance pulmonaire globale a physiopathologie et son traitment J International de Chirurgie du Thorax 1949 *1* 35
WEST J R McCLEMENT J H CARROLL D BLISS H A KUSCHNER M RICHARDS D W JR and COURNAND A Effects of Cortisone and ACTH in Cases of Chronic Pulmonary Disease With Impairment of Alveolar Capillary Diffusion Am J Med 1951 *10* 156

# DISEASES OF THE LUNGS

By J WINTHROP PEABODY M D and J WINTHROP PEABODY JR M D

## PULMONARY CONGESTION AND EDEMA

### PULMONARY CONGESTION

Congestion of the lungs follows acute inflammatory lesions such as those caused by pneumonia respiratory obstruction and over rapid expansion of a collapsed lung or it may follow acute circulatory failure caused by left ventricle failure congenital heart disease mitral stenosis, or systemic diseases associated with fluid retention in the lungs or other organs It may be difficult to determine whether the severe dyspnea is due to a primary pulmonary inflammation or to congestion from cardiac disease If a few days of rest and the use of mercurial diuretics fail to alleviate the symptoms, pulmonary insufficiency may be considered the cause Measurement of circulation time is diagnostic in cardiac studies for the velocity of circulation is not impeded in uncomplicated pulmonary congestion However both pulmonary and cardiac insufficiency may be coexistent particularly in ventricular failure

*Acute congestion* (hyperemia) of the lungs may follow inhalation of a foreign body or irritating gases shock infections, trauma and vascular and hemorrhagic diseases It may last for a few minutes or for several hours It becomes severe when transudates fill the alveoli The circulation in the affected area is slowed down fluid floods the lung reabsorption is interfered with and edema develops The prognosis is grave A collateral hyperemia sometimes occurs when a lung obstruction is present or as the result of a rapidly developing pleural effusion, a spreading pneumonia or a pneumothorax

*Chronic passive congestion* follows any obstruction to free flow of blood from the lungs to the heart whether this is due to cardiac vascular pulmonary or extrapulmonary disease The most frequent causes are hypertensive heart disease and rheumatic mitral valvulitis aortic regurgitation stenosis and myocardial infarction Obstruction to pulmonary circulation may also arise from pulmonary diseases such as hypertrophic pulmonary emphysema fibrosis sclerosis atelectasis pneumoconiosis chronic abscesses bronchiectasis and tumor

*Hypostatic passive pulmonary congestion* occurs in the lower posterior area of the lungs in patients with prolonged infections cerebral apoplexy in elderly patients long confined to bed and in those in prolonged coma It may also occur in any chronic state causing interference with respiration Such interference resulting in stagnation of blood

in the dependent areas of the lungs is therefore unlike a mechanical congestion. In a prolonged hypostatic congestion resistance of the lung to infection decreases and a low-grade pneumonia may develop. To prevent this condition Cecil advises deep-breathing exercises for the asthenic or debilitated patient, changing the patient's position in bed or having him sit up in a chair, and improving his morale by use of psychotherapy, physiotherapy, and proper diet.

Pulmonary congestion leads to edema when the serous fluid of the capillaries escapes into the parenchyma and bronchial tree and involves one or both lungs.

## Pulmonary Edema

*Etiology.*—Pulmonary edema and anoxia are so closely associated that it is difficult to determine which precedes the other; severe anoxia may cause pulmonary edema; pulmonary edema may cause or aggravate anoxia. The edema may result from left-ventricular failure secondary to disease of *the coronary artery, arterial hypertension,* aortic stenosis or insufficiency, or mitral disease; from congenital heart disease; from pulmonary diseases associated with capillary damage or hemodynamic alterations in the lung produced by obstructive emphysema, gaseous irritants, pulmonary infarction, or polycythemia vera; or from systemic diseases associated with fluid retention in the lung or other organs. Acute pulmonary edema may be a complication of acute infectious disease, poisoning by various substances or asphyxiating gases, or disease of the central nervous system (such as cerebral trauma, myelitis, or cerebral embolism or thrombosis) and commonly follows shock.

*Pathogenesis.*—Edema is produced by imbalance between the osmotic pressure of the plasma proteins and the capillary blood pressure. The capillaries, unlike the venous and arterial vessels, do not form a continuous channel but rather a network providing a safety valve to prevent undue increases of pressure. This balance of pressure is never quite perfect, being always just at the edge of fairly free protein leakage. When dyspnea is present, the negative intrapleural pressure is much increased, particularly if the respiratory passage is restricted by some exudation. However, if the circulation remains adequate, a certain degree of anoxia can be withstood normally, without causing edema.

The thin alveolar membrane and the delicate capillary endothelium are all that separate blood from air in the lung tissues and are the only barrier to transudation of fluid from the blood vessels into the tracheobronchial tree. Any affection tending to increase the pressure within the capillaries or to decrease the pressure within the air channels will in turn increase the transudation through the intervening membrane. Although the permeability of the capillary walls is increased by anoxia, with further leakage of protein and water into the pulmonary tissue, if the circulation remains fairly good, the lymphatic system can successfully remove the leakage before the fluid penetrates the alveolar walls and invades the air spaces. On the other hand, when the circulation is impaired, fluid in the alveolar walls passes directly into the alveolar air *spaces and exerts mechanical impediment* to the passage of water to the capillaries, and anoxia begets anoxia.

With mechanical obstruction to the alveoli from seepage of fluid into the airway and resultant interference with free circulation of air, the lung solidifies. The interstitial structures thicken, and loss of elasticity in the pulmonary tissues prevents free expansion and contraction of the lung. This in turn leads to impairment of the normal physiologic mechanism controlling the rate and depth of respiration. Rapid or shallow breathing causes incomplete aeration and anoxia, and the resultant pulmonary edema causes a reduction in the oxygen saturation of the arterial blood and so increases the anoxia.

*Clinical Features.*—In pulmonary edema a variable degree of dyspnea is noted initially together with hacking cough and pinkish sputum. Cheyne-Stokes respiration and cyanosis are noted in advanced cases. In cases of left ventricular failure attacks of paroxysmal dyspnea occur with cough and wheezing ("cardiac asthma"). Roentgenologic findings in pulmonary edema vary depending on the acuteness or chronicity of

the condition and on associated pulmonary affections

*Treatment* —Medical treatment includes rest warmth, reduction of fluid intake, the use of digitalis mercurial diuretics, sedation, and venesection *Oxygen therapy is of* the greatest importance and should be administered before the occurrence of serious respiratory and circulatory decompensation When given after dyspnea cyanosis and moist rales develop oxygen may not prevent irreversible pulmonary edema (When pulmonary edema is associated with pneumonia 50 cc of 50 per cent glucose injected intravenously for 2 or 3 days at intervals of from 8 to 12 hours may be of value ) Venesection 250 to 500 cc is favored by most authors unless there is shock The use of aminophylline, 0 24 Gm by slow intravenous administration is recommended Morphine sulfate in 15 mg (1/4 grain) doses is proposed for lowering the excitability of the nervous system except in cases of collapse

REFERENCES


BARACH A I Physiologic Therapy in Respiratory Diseases Philadelphia J B Lippincott Co 2d ed 1948

DRINKER C K *Pulmonary Edema and Inflammation* Cambridge Mass 1946 Harvard Univ Press

HINSHAW H C Pulmonary Edema and Congestion In MYERS J A and McKINLAY C A The Chest and the Heart Springfield 1948 *Charles C Thomas v 1*

RHOADS P S Pulmonary Edema In KYSER F A Therapeutics in Internal Medicine New York 1950 Thomas Nelson Co 1950


## PULMONARY HEMORRHAGE

Hemorrhage of the lung a common symptom in pulmonary disease may result in only occasional streaking of the sputum or may be (1) intermittent bleeding which if continued may lead to blockage of the bronchial tree, atelectasis and exsanguination or (2) fatal massive hemorrhage from the rupture of a blood vessel

During hemorrhage the blood may escape into a bronchus or a pulmonary cavity and be expectorated in the liquid state or it may be temporarily retained and expectorated *later in clots* On the other hand, the blood may pass into the alveolar *or interstitial* tissues or may rupture the capillary walls and be expectorated as reddish or brownish sputum When less than 4 cc are expectorated, the term hemoptysis is used rather *than hemorrhage*

Profuse hemorrhage occurs more often in chronic than in acute pulmonary disease Hemorrhage occurs about equally in both lungs and equally in all lobes, sometimes it is bilateral The bronchi and any rigid cavity crossed by thrombosed blood vessels are the usual sources of the bleeding Bleeding may result from pulmonary diseases such as bronchial ulceration or compression tuberculosis, bronchial carcinoma bronchiectasis and pulmonary abscess Other occasional causes of pulmonary hemorrhage are blood dyscrasias vitamin deficiencies altering the structure of the blood vessels foreign bodies, trauma, cardiac diseases associated with mitral stenosis hypertension and arteriosclerosis, pneumonia and bronchial adenoma

*The symptoms attending hemorrhage* are those of the underlying disease in 90 per cent of cases

*Treatment* —Slight hemoptysis requires no attention except determination of the underlying cause Efforts must be made to allay the patient s alarm if the bleeding is profuse Sedatives may be administered but strong opiates particularly morphine which may interfere with cough reflex and depress the respiratory center should be withheld Bed rest is essential The head should be propped up with pillows to facilitate free breathing and expectoration If the bleeding is profuse intravenous injection of 10 per cent calcium gluconate solution has been recommended Pneumothorax may be used if the site of bleeding can be determined

Blood transfusion is indicated for severe loss of blood Usually medical treatment is of no avail The hemorrhage may stop spontaneously

REFERENCES


ABBOTT O A Clinical Significance of Pulmonary *Hemorrhage Study of 1 316 Patients With* Chest Disease Dis Chest 1948 *14* 824

RYAN T C and LINEBERRY W T JR Pneumonectomy for Pulmonary Hemorrhage in Tuberculosis Am Rev Tuberc 1950 *61* 426

Sokoloff M Symptomatic Management of Pulmonary Tuberculosis Gen Practitioner 1951 3 67

## PULMONARY EMBOLISM AND INFARCTION

*Incidence* — About 6 per cent of all post operative deaths are due to pulmonary embolism (Barnes) and the incidence is increasing annually This may be due to the increasing number of older patients with cardiovascular degenerative processes promoting thrombosis and embolism to the increasing number of older persons having major operations and to the steadily increasing number of accidents leading to long confinement in bed and immobility of the limbs Thromboembolism occurs equally in both sexes

*Etiology* —Prolonged bed rest is one of the chief causes of pulmonary embolism since it favors the development of phlebothrombosis But thrombi in the right ventricle or in the right auricle or thrombi from vegetations on the valves of the right side of the heart may also cause such embolism Moran has found pulmonary embolism a frequent complication of tuberculosis

*Clinical Features* —When a blood clot is dislodged from its point of origin it is carried to the lungs by way of the heart and if large may lodge in the pulmonary artery and cause sudden death by obstructing the flow of blood through the lung and producing heart failure If the embolus is small it may block a smaller blood vessel or may split into small emboli which reach the terminal ramifications

When the embolus is massive the patient is seized with severe pain in the chest and extreme dyspnea become blue in the face, and dies within a few minutes

The general symptoms are rise in temperature and pulse rate and in the few nonfatal cases dyspnea perspiration paleness lowered blood pressure and an apprehensive appearance Cough and hemoptysis may occur Pleuritic pain with exaggerated dyspnea is a common symptom of a small pulmonary embolus pleural effusion follows a few hours later These symptoms particularly after a major operation suggest embolism These early symptoms often imitate those of primary cardiac disease differentiation is sometimes made by electrocardiographic studies

Pulmonary infarction almost always occurs as a result of sudden occlusion of a branch of the pulmonary artery The symptoms depend on the size of the occluded blood vessel the status of the pulmonary circulation the degree of restriction of blood flow through the lungs and the number of emboli The symptoms are dyspnea cyanosis apprehension and some degree of shock with chest pain fever cough and hemoptysis Sometimes the lung on percussion sounds dull or flat auscultation sometimes discloses a friction rub or rales Pleural effusion at times hemorrhagic is occasionally found

*Radiologic Findings* —The characteristic radiologic finding of pulmonary infarction is a wedge shaped homogenous density As healing occurs the density become smaller and presents a transverse linear appearance often confused with plate like atelectasis pleurisy or postoperative pneumonia

*Treatment* —Treatment is almost entirely preventive The physiologic cause of the pulmonary embolism is a disproportion between prothrombin and antithrombin in the blood A clot may occur even when the prothrombin level is low if the antithrombin content is proportionally lower Following tissue injury of whatever cause the antithrombin content of the blood is diminished and this may bring about a disproportion between prothrombin and antithrombin sufficient to produce a thrombosis if the antithrombin level does not return to normal within a few days For this reason prophylactic anticoagulants are rather widely used in cases in which a thrombosis may be anticipated The use of these agents is also indicated for treatment of pulmonary embolism and infarction (*See* Chapter 24 )

## REFERENCES

Baker D V *et al* Pulmonary Embolism Evaluation of Policy for Prophylaxis and Therapy New England J Med 1950 *242* 923

Barnes A R Problem of Pulmonary Embolism West J Surg 1942 *50* 551

*the condition and on associated pulmonary* affections

*Treatment* —Medical treatment includes rest warmth reduction of fluid intake, the use of digitalis mercurial diuretics sedation and venesection Oxygen therapy is of the greatest importance and should be administered before the occurrence of serious respiratory and circulatory decompensation When given after dyspnea cyanosis and moist rales develop oxygen may not prevent irreversible pulmonary edema (When pulmonary edema is associated with pneumonia, 50 cc of 50 per cent glucose injected intravenously for 2 or 3 days at *intervals of from 8 to 12 hours* may be of value) Venesection 250 to 500 cc is favored by most authors unless there is shock The use of aminophylline 0 24 Gm by slow intravenous administration is recommended Morphine sulfate in 15 mg (¼ grain) doses is proposed for lowering the excitability of the nervous system except in cases of collapse

REFERENCES


BARACH A I Physiologic Therapy in Respiratory Diseases Philadelphia J B Lippincott Co 2d ed 1948

DRINKER C K Pulmonary Edema and Inflammation Cambridge Mass 1946 Harvard Univ Press

HINSHAW H C Pulmonary Edema and Congestion In MYERS J A and MCKINLAY C A The Chest and the Heart Springfield 1948 Charles C Thomas v 1

RHOADS P S Pulmonary Edema In KYSER F A Therapeutics in Internal Medicine New York 1950 Thomas Nelson Co 1950


## PULMONARY HEMORRHAGE

Hemorrhage of the lung a common symptom in pulmonary disease may result in only occasional streaking of the sputum or may be (1) intermittent bleeding which if continued may lead to blockage of the bronchial tree atelectasis and exsanguination or (2) fatal massive hemorrhage *from the rupture* of a blood vessel

During hemorrhage the blood may escape into a bronchus or a pulmonary cavity and be expectorated in the liquid state or it may be temporarily retained and expectorated later in clots On the other hand, the blood may pass into the alveolar or interstitial tissues or may rupture the capillary walls and be expectorated as reddish or brownish sputum When less than 4 cc are expectorated, the term hemoptysis is used rather than hemorrhage

Profuse hemorrhage occurs more often in chronic than in acute pulmonary disease Hemorrhage occurs about equally in both lungs and equally in all lobes, sometimes it is bilateral The bronchi and any rigid cavity crossed by thrombosed blood vessels are the usual sources of the bleeding Bleeding may result from pulmonary diseases such as bronchial ulceration or compression, tuberculosis bronchial carcinoma, bronchiectasis and pulmonary abscess Other occasional causes of pulmonary hemorrhage are blood dyscrasias vitamin deficiencies altering the structure of the blood vessels foreign bodies, trauma, cardiac diseases associated with mitral stenosis hypertension and arteriosclerosis, pneumonia and bronchial adenoma

The symptoms attending hemorrhage are those of the underlying disease in 90 per cent of cases

*Treatment* —Slight hemoptysis requires no attention except determination of the underlying cause Efforts must be made to allay the patient s alarm if the bleeding is profuse Sedatives may be administered but strong opiates particularly morphine which may interfere with cough reflex and depress the respiratory center should be withheld Bed rest is essential The head should be propped up with pillows to facilitate free breathing and expectoration If the bleeding is profuse intravenous injection of 10 per cent calcium gluconate solution has been recommended Pneumothorax may be used if the site of bleeding can be determined

Blood transfusion is indicated for severe loss of blood Usually medical treatment is of no avail The hemorrhage may stop spontaneously

REFERENCES


ABBOTT O A Clinical Significance of Pulmonary Hemorrhage Study of 1 316 Patients With Chest Disease Dis Chest 1948 *14* 824

RYAN T C and LINEBERRY W T JR Pneumonectomy for Pulmonary Hemorrhage in Tuberculosis Am Rev Tuberc 1950 *61* 426

largement of the heart or by pressure on the base of the lung by abdominal growths subdiaphragmatic abscess or ascites In pleural effusion and in pneumothorax the uniform collapse producing symptoms is due to reduction of the aerating surface and to mediastinal displacement and cardiac embarrassment

Although the shrunken portion of the lung may exist for many years without impairment of pulmonary function and suddenly re-expand the retracted bronchial tree may become permanently distorted and this may result in defective drainage stagnation and ultimate infection The process then becomes irreversible and fibrosis and bronchiectasis develop

*Obstructive atelectasis* occurs in many intrathoracic affections in which bronchial obstruction is a common factor (*See* page 879)

As a result of the secretion and caseous material in their bronchi constriction of the bronchi due to endobronchial tuberculosis and fibrosis and the pressure caused by lymph nodes and tuberculomata, as well as the compression of pulmonary tissue by collapse therapy, tuberculous patients are particularly predisposed to atelectasis

Massive collapse occurs when there is a gross bronchial obstruction with paralysis of the muscles as in diphtheria Postoperatively or in case of trauma to the chest acute massive atelectasis may occur Massive atelectasis may also follow any sudden obstruction of the bronchi pulmonary infarction infection and allergic attacks

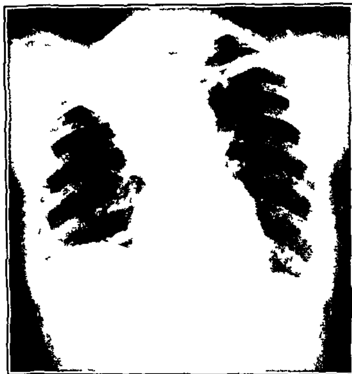


FIG 1?0 —Atelectasis in right upper lobe with endobronchial disease

Complete obstruction followed by absorption of gases and maximum retraction of the involved area usually occurs within a few hours if however there has been previous inflammation of lung tissue in the affected area the gas absorption is less marked and the retraction occurs more slowly The collateral circulation of gases may partially maintain the inflation of the lung if the bronchial obstruction is not extensive

Postoperative atelectasis may follow any operation which causes interference with

HINSHAW H C Pulmonary Embolism In MYERS J A and McKINLAY C A Chest and Heart Springfield Charles C Thomas v 1 1948

OCHSNER A Newer Concepts of Blood Coagulation With Particular Reference to Postoperative Thrombosis Ann Surg 1950 131 652

## PULMONARY ARTERIOSCLEROSIS

*Etiology* —Pulmonary arteriosclerosis is a rare disease that may be either a manifestation of a generalized arteriosclerosis of the entire vascular system or a consequence of hypertension of the lesser circulation The disease may be primary without preceding lung or heart disease (Ayerza s disease), or secondary attendant upon some long standing condition such as bronchiectasis pneumoconiosis tuberculosis congenital cardiac or thoracic abnormality cardiovascular disease emphysema or asthma When the disease is primary there is arterio-capillary fibrosis of the lung with obliteration and angutis of the smaller arterioles when the disease is secondary there is a widespread sclerosis of the larger branches of the pulmonary artery

*Clinical Features* —Usually the patient reports having had a cough with mucopurulent expectoration over a period of years dyspnea on exertion and recurrent attacks of bronchitis Headache somnolence hemoptysis and precordial pain may be noted As the disease progresses edema is indicative of a right-ventricular failure and increased venous pressure with dilatation and hypertrophy of the right side of the heart and of the superficial veins is apparent Cyanosis is usually marked the patient s hands and face becoming almost black (Black cardiac) The fingers may show definite clubbing Other pathologic changes include enlargement of the liver lowered renal function and infarction of the lungs Radiologic studies often reveal prominence of the pulmonary conus and artery and enlargement of the right ventricle Oblique views afford better demonstration hypertrophy of the body of the right ventricle being demonstrated in the left anterior view and enlargement of the outflow tract and conus in the right anterior view Pulmonary arteriosclerosis may be differentiated from polycythemia vera by its respiratory symptoms, absence of any splenic enlargement, and signs of general passive congestion The condition may endure for many years Death often results from myocardial failure or from an intercurrent infection

*Treatment* — Treatment consists in symptomatic relief, attempts to relieve the underlying causes, which are often not amenable to therapy, and the management of congestive heart failure by the usual means of rest diet oxygen digitalis, and diuretics The prognosis in this type of heart failure is considerably worse than in general heart failure

*REFERENCE*

RUBIN I H and RUBIN M Diseases of the Chest Philadelphia W B Saunders Co 1947

## ATELECTASIS

*Definition* — Atelectasis is incomplete expansion of the lung It occurs when an air passage is completely or almost completely occluded and non aeration of the alveoli of some unit of the lung which has no collateral respiration through communication with some other air passage results

*Types of Atelectasis* —Three types of atelectasis are recognized congenital compressive and obstructive

Congenital atelectasis is caused by absence of alveoli mechanical obstruction of the bronchi by amniotic fluid or inflammatory processes that prevent complete unfolding of alveolar tissues Such atelectasis may cause death at birth or if the occlusion is minor produce a blue baby Recovery may be spontaneous or may require artificial aspiration of the occluding fluid or mucus Unless the occluded areas become infected compensating areas may prevent development of symptoms and the growing child may recover without diagnosis of the condition If atelectasis continues bronchiectasis may develop

*Compressive or adjustment atelectasis* is due to pulmonary retraction where the peripheral support of the lung is inadequate or there is reduction of the thoracic volume The pressure may be produced by thoracic deformities by pericardial effusion by en

fected pulmonary areas are already over-functioning

When the breathing is shallow and cyanosis and dyspnea are present inhalation of 50 to 70 per cent oxygen may be required to maintain respiratory function This may be administered by oxygen tent oxygen mask or nasal catheter Catheter suction to evacuate the exudates has been recommended If this cannot be instituted or is ineffective bronchoscopic aspiration should be attempted Penicillin or some other antibiotic should be introduced into the bronchial tree after the evacuation of the exudates

It must be remembered that these measures may not be required in simple or lobular atelectasis as these cases often clear up spontaneously the physical postoperative measures already described may suffice

Treatment of atelectasis other than postoperative is that of the primary disease

REFERENCES

ADAMSON J D Pulmonary Atelectasis In MYERS J A and MCKINLAY C A Chest and Heart Springfield Charles C Thomas v 1 1948

BARACH A L Physiologic Therapy of Respiratory Diseases Philadelphia J B Lippincott Co 1948

CHRISTIE H E MEAKINS J F and ARONOVITCH M Aerosol Therapy in Treatment of Postoperative Pulmonary Atelectasis Canad M A J 1949 *61* 388

COULTER W W Experimental Massive Pulmonary Collapse Dis Chest 1950 *18* 146

HAYES E W and HAYES E W JR Atelectasis In BANYAI A L Nontuberculous Diseases of the Chest Springfield Charles C Thomas *In Press*

## EMPHYSEMA

*Definition* —Pulmonary emphysema is a disease in which there is an interference with the normal functioning of respiration and circulation with subsequent dilatation and rupture of the alveoli and decreased elasticity of the involved lung Five general types are recognized (1) obstructive or hypertrophic emphysema (2) compensatory emphysema (3) senile or atrophic emphysema (4) interstitial emphysema and (5) progressive bullous emphysema The *chronic* or hypertrophic type is generally meant when emphysema of the lung is discussed

Although the disease has been reported in infants only three weeks old it occurs most often in males of middle age or over who have a history of chronic respiratory obstruction following asthma chronic bronchitis chronic cough from tuberculosis bronchiectasis or pneumoconiosis The disease may occur suddenly in an apparently healthy person who several months before recovered from an atypical pneumonitis or bronchial asthma

*Etiology and Pathogenesis* —The chief etiologic factor in emphysema is chronic interference with the free passage of air in the bronchi

It is generally agreed that loss of elasticity in the pulmonary tissues either by infection or atrophy is the chief factor in disturbance in respiratory function in this disease

With loss of elasticity, the air sacs are distended Bullæ appear on the surface of the lung as the superficial air sacs are stretched to a greater extent than those situated deep in the lung since the greatest expansion is at the surface of the lung With increased stretching of the alveolar walls the air sacs are joined the walls themselves torn and the pulmonary capillaries destroyed so that large areas have a diminished circulation of blood Moreover a negative pressure within the chest normally facilitates the return flow of venous blood to the heart in emphysema the negative pressure is lost through inelasticity of the structures and the pressure may even be positive during expiration thereby impeding the return flow of blood and bringing about an elevation of venous pressure If the pressure is sufficiently great the air may be forced into the subcutaneous tissues or into the pleural cavity and produce a pneumothorax that is if alveoli or blebs are ruptured

Another effect of reduced elasticity is interference with the exchange of gases in the lungs another is an increased amount of residual air which keeps the alveoli distended The residual air accumulates at the expense of vital capacity which may be diminished to less than half of normal The decreased vital capacity may approximate the resting tidal air so that the

pulmonary drainage Sedation, suppression of cough and expectoration because of pain, fixation of the diaphragm and keeping the patient long in one position cause stagnation secretions of the upper respiratory tract are added to pulmonary secretions Postoperative atelectasis may involve an entire lung a single lobe or only part of a lobe

*Clinical Features* —The manifest symptoms of atelectasis are usually those of the primary disease Except for a rapid pulse postoperative atelectasis is often symptomless and without *x* ray examination will not be suspected When two or three days after operation a patient has difficulty in raising sputum shows a slight increase in temperature and exhibits poor aeration of the lower lobe together with coarse rales at the bases atelectasis should be considered In severe cases there may be high fever prostration distressing cough chest pain, dyspnea and tachycardia suggestive of lobar pneumonia except that the heart is displaced to the affected side and the sputum is seldom bloody The affected side of the thorax may be found to be immobile and the breath sounds may be diminished or absent

Usually collapse occurs in the lower areas of the lungs Diminished or absent breath sounds are noted over those regions with lessening of the normal resonance on percussion and fine crackling rales during inspiration Displacement of the heart toward the affected side will be noted

Radiologic findings vary according to the extent of the atelectasis The opacity is dense and covers a large area in gross collapse the heart trachea and mediastinum are displaced toward the affected side and the diaphragm is found to be elevated

*Differential Diagnosis* —Atelectasis is differentiated from pneumothorax and pleural effusion by the position of the heart and the mediastinum which in massive collapse are drawn toward the affected side they are displaced to the opposite side in pleural effusion and pneumothorax The presence of fever and the physical signs of atelectasis may suggest pneumonia but the displacement of the heart, mediastinum, and diaphragm will rule out pneumonia Pulmonary embolism may be suspected but hemoptysis is absent in atelectasis, and shock and pain are less severe

*Prognosis* —The prognosis in atelectasis is generally good the condition disappearing in a few days unless the primary affection is serious or chronic In such cases, and in those in which pneumonia or abscess develops the atelectasis may become bilateral and persistent

*Treatment* —Treatment of postoperative atelectasis is preventive Every effort must be made to prevent accumulation of secretion in the bronchial tree Movements of the diaphragm and lower ribs must not be restricted and the cough reflex must not be inhibited

Operations should be postponed if possible when infection of the upper respiratory tract is present Patients with chronic bronchitis are best operated on during the summer Elderly and feeble patients should be encouraged to walk about for several weeks before operation

At operation, the patient should be placed in a position to facilitate drainage The anesthesia should be as light as possible During the operation the upper air passage should be kept free from excessive secretion by frequent aspiration with a rubber catheter

Postoperative therapy is directed to removal of accumulated secretions and keeping the air passages clear Using the Trendelenberg position turning the patient from side to side at intervals, encouraging deep breathing and expectoration avoidance of tight bandaging and early ambulation are all suggested measures

Inhalation of a mixture of 5 per cent carbon dioxide and 95 per cent oxygen at intervals of from 2 to 4 minutes is recommended to expand the bronchial walls and stimulate the cough reflex Oxygen alone tends to increase the viscosity of the secretions causing them to adhere to the bronchial membranes Inhalation of steam has been found to overcome the disadvantages of the oxygen in the carbon dioxide mixture steam inhalation is also more effective in liquefying the exudate than the ordinary expectorants When symptoms of respiratory distress are marked stimulation of respiration by carbon dioxide is contraindicated since the unaf

compensates for impaired function of another segment Increase in the size of the alveoli does not necessarily increase their function and their permanent distention tends to impair the thoracic bellows although in some instances readjustment may occur without pathologic emphysema In unilateral compensatory emphysema the emphysematous side will appear more prominent and mobile vocal fremitus will be relatively small the position of the diaphragm and its mobility are relatively normal In senile emphysema the activity of the abdomen is greater than that of the chest wall

*Interstitial emphysema* develops upon rupture of the marginal alveoli by trauma or by violent coughing The air either passes into the subpleural space or the peribronchial or perivascular tissues or passes along the



Fig 151 —Emphysema in upper left lobe

diminished hyperresonance will be noted and breath sounds exaggerated

*Senile atrophic or postural emphysema* is a disease of old age The distention is generally considered due to stiffness of the spine rather than to loss of elasticity The lung tissue is wasted the ribs become more horizontal as the vertebral bodies become fixed and with degeneration of the disks the thoracic spine becomes kyphotic so that the chest assumes a barrel shape It is a nonobstructive emphysema the lungs are

pleura and enters the mediastinum from which it travels along the trachea to invade the subcutaneous tissues of the neck Mediastinal emphysema is more apt to result from rupture of pulmonary alveoli after operations on the neck than from direct aspiration of air into the mediastinum Postmortem examination has shown extensive subcutaneous emphysema over the front of the chest with the air bubbles arranged like a string of pearls and the heart

patient although comfortable in bed will be dyspneic upon the slightest exertion In this case the alveolar air and the arterial blood contain more carbon dioxide and less oxygen than is normal the saturation of oxygen in the blood sometimes becoming as low as 60 per cent, which would cause a normal person to become unconscious whereas the emphysematous patient may show no ill effects Impairment of carbon dioxide elimination is considered due not only to inability of the patient to increase pulmonary ventilation but also to the unequal ventilation of the lung much of the inspired air being wasted in ventilating the superficial alveoli which have become overstretched avascular, and relatively functionless

*Symptoms and Signs* —The symptoms may arise suddenly in infancy or have an *insidious onset in later life* The most constant symptom is shortness of breath often accompanied by cyanosis of a severity that the physical signs do not seem to justify Cyanosis is due to the inability to aerate the blood but *compensatory polycythemia* is also a contributing factor

Most patients have a chronic cough Expiration is prolonged sometimes being four times the length of inspiration However this sign is not pathognomonic of emphysema as it is frequently noted in men of middle age or over The barrel shaped chest of the patient is a characteristic sign The ribs are elevated and tend to lie horizontally the costal angle is increased the chest is elevated and its expansion restricted Hyperresonance is noted on percussion chest expansion is decreased breath sounds are weak heart sounds are soft and distant and vocal fremitus is diminished

An increased carbon dioxide level in the blood may be demonstrated Measurements show the vital capacity is diminished

Radiologic examination may show characteristic changes in the lungs but these are not always present *Increased aeration* may be noted unless there is considerable fibrosis The diaphragm appears depressed flattened and restricted in motion Translucency of the lung is increased and the hilar shadows are accentuated Blebs or bullae may cast annular transparencies and resemble tuberculous cavitations

*Treatment* —Treatment of emphysema is entirely symptomatic, since neither elasticity of the tissues nor the structure of the chest can be restored The disease is usually slowly progressive and, because of its associated bronchitis may become disabling Since it is incurable the patient must follow a careful regime of rest diet, and exercise avoid exposure to sudden changes in temperature and keep within his physical limitations It is important that concurrent diseases such as bronchitis and asthma be treated Bronchial spasm may be relieved and dyspnea therefore lessened by administration of ephedrine in doses of ⅜ to ¾ grains Aminophylline 0 5 gram in rectal suppositories has been recommended Nebulized epinephrine may lessen purulent expectoration Inhalation of oxygen alone is helpful *during dyspneic attacks the dyspnea being* due to difficulty in transmitting oxygen to the arterial blood not to impairment of carbon dioxide elimination Continuous inhalation of 50 per cent oxygen sometimes *brings progressive or complete relief* of dyspnea, if the patient can continue in the oxygen-enriched atmosphere for a period of from 2 days to 1 week Patients with associated pulmonary fibrosis may be helped by this treatment but require continued oxygen at home Barach recommends inhalation of 100 per cent pure oxygen in a mask for 20 or 30 minutes daily in these cases Intermittent positive pressure breathing (I P P B ) according to the method of Motley *et al* may afford symptomatic relief in emphysema

Use of an abdominal belt has been recommended especially in patients with sufficient adipose tissues to increase intra abdominal pressure by elevating and supporting the diaphragm Respiratory exercises to teach patients to deflate the lungs and increase the use of the diaphragm is sometimes advocated

*Pneumoperitoneum* which has been extensively used in treatment of tuberculosis is receiving favor in therapy of emphysema

## OTHER TYPES OF PULMONARY EMPHYSEMA

*Compensatory emphysema* is a condition in which dilatation of one part of the lung

The walls of the acute abscess are soft and friable, those of the chronic abscess are fibrous and smooth. Lung abscesses may increase by direct extension or by a spreading of the infective material through neighboring bronchi. When the protective wall of the abscess breaks down and becomes necrotic the inflammatory process extends to the surface of the lung and causes an empyema or a gangrenous pneumonia.

*Symptoms.*—The symptoms of lung abscess vary according to the site and stage of the disease and the degree of bronchiectasis and consolidation in surrounding tissue. The first manifestations may be chills with fever followed by coughing and expectoration. If the onset of the disease is sudden there may be profuse sweating and prostration. The cough increases with progress of the abscess, and expectoration of a large quantity of foul sputum indicates rupture of the abscess into a bronchial ramification—the only true pathognomonic symptom. Periodically, the sputum may be streaked with blood. Pleuritic pain may occur in the initial stage of the disease. Sepsis is demonstrated by a high sedimentation rate and a leukocytosis. In cases with a slow onset there may be a secondary anemia and hypoproteinemia. Some patients with chronic lung abscess suffer from general malaise, aching of the musculature, and loss of both weight and strength. Cyanosis and clubbing of the digits may develop suddenly.

*Diagnosis.*—No signs are revealed on palpation if the lung abscess is small and deeply located. Increased tactile fremitus may be noted if the abscess is large and the adjacent tissues are extensively inflamed; the fremitus may be decreased or absent if pleuritic exudates are present. Chronic cases show decreased movements of the thorax and atrophy of the chest muscles. The percussion note is variable; over large abscesses there may be bronchial breathing.

Roentgen findings depend on the extent of the inflammatory process. The roentgenologic findings in general are typical of many other pulmonary infections. In the early stages small areas of infiltration may be revealed which remain rather clearly demarcated even when the area increases and becomes denser. A definite fluid level is often observed.

The bronchogram is of value in distinguishing between an abscess and a bronchiectasis. Bronchoscopy may demonstrate the location of the abscess, by indicating from which bronchus pus is exuding, and may also give evidence of obstruction. Bronchoscopy is used to remove tissue for determination of malignancy.

Lung abscess must be differentiated from empyema rupturing into a bronchus, bronchiectasis, cystic disease of the lung, pulmonary tuberculosis, cancer of the lung, and fungus disease.

*Treatment.*—Poor results in treatment have generally been due to late diagnosis and too conservative therapy. Medical treatment includes postural drainage, chemotherapy including the use of antibiotics, and bronchoscopic aspiration. Surgical therapy includes lobectomy or segmental resection and, in severe cases, pneumonectomy. Drainage by pneumonotomy or pleurotomy suffices in some cases.

Conservative treatment includes rest in bed and a nutritious diet, supportive therapy, and postural drainage. The use of aureomycin, streptomycin, or sulfadiazine to supplement penicillin may bring results comparable to those of early surgical drainage and make resection unnecessary. In acute abscesses aerosol therapy may be beneficial.

*Prognosis.*—Until the last decade prognosis in cases of pulmonary abscess was poor, the mortality rate being between 30 and 50 per cent. Greater use of lobectomy and pulmonary resection has resulted in fewer deaths.

Between 20 and 35 per cent of all lung abscess victims are said to have spontaneous recoveries.

*Preventive Treatment.*—Preventive measures are important in reducing the incidence of lung abscess. Since a predominating cause of pulmonary abscess is aspiration of infectious material, daily oral hygiene is important, as is special oral hygiene before the administration of any anesthetic. Local anesthesia is preferable for operations on the mouth or throat, since such anesthesia does not inhibit the cough reflex. Where general anesthesia is required, the patient's head

and large blood vessels surrounded by air bubbles

The symptomatology depends on the degree of circulatory embarrassment caused by pressure of the air bubbles on the vessel sheaths and the degree of respiratory impediment caused by the pressure of the air on the interstitial tissues Dyspnea and cyanosis may be observed, and retrosternal pain of short duration radiating to the neck and shoulders The symptoms may imitate those of pericarditis, pulmonary infarction, pneumonia or coronary thrombosis Unless subcutaneous emphysema is present, hyperresonance may be noted over the affected side on percussion with obliteration of cardiac dullness Crackling bubbling or crunching sounds (Hamman s sign) may be heard in the chest even without the aid of a stethoscope No therapy is required if the aberrant air in the interstitial tissues is small and unaccompanied by distressing symptoms Mediastinal pressure makes the condition serious Oxygen inhalation is recommended for dyspnea opiates for painful cough, and antibiotic therapy for secondary infections

*Bullous emphysema* a collection of distended vesicles forming large air pockets within the lung It may be a sequel to bronchial obstruction in childhood following bronchopneumonia, influenza or other acute infections, to aspiration of foreign bodies or to bronchiolitis from noxious gases It is frequently associated with fibrous tuberculosis, pneumoconiosis bronchogenic neoplasms and chronic pneumonitis Nonexpansile bullæ present no problem unless infection occurs or they are mistakenly diagnosed as spontaneous pneumothorax They may cause pressure on the surrounding tissues, may rupture or may cause recurrent pneumothoraces

No effective therapy has been devised and the prognosis is grave although some patients with the condition live for a number of years

REFERENCES


ABRAMSON H ROOK G D and NAU C H Acute Pulmonary Interstitial and Mediastinal Emphysema (Airblock) and Pneumothorax in Infancy and Early Childhood J Pediat 1950 *38* 774

BARACH A L Physiological Methods in Diagnosis and Treatment of Asthma and Emphysema Ann Int Med, *1938*, *12*, 454

CHRISTIE R V Emphysema of the Lung Brit M J 1944, *1*, 105 143

COOPE ROBERT Diseases of the Chest Baltimore Williams & Wilkins Co 2d ed 1948

FURMAN R H and CALLAWAY J J Artificial Pneumoperitoneum in the Treatment of Pulmonary Emphysema Dis Chest, 1950, *18* 23?

HAMMAN, LOUIS Mediastinal Emphysema J A M A 1945 *128* 1


## LUNG ABSCESS

*Definition* —A pulmonary abscess is an inflammatory process within the parenchyma of the lung in which there is some cavitation with free purulent fluid and necrosis Lung abscesses may be single or multiple and may involve either or both lungs Lung abscesses are called *simple* or *complex* according to the degree of involvement of the surrounding tissues and they may be acute or chronic, putrid or nonputrid

*Incidence* —These abscesses occur in persons of all ages, 50 per cent of the victims however are between 20 and 40 years old Such abscesses occur twice as frequently in men as in women Lung abscesses in children usually follow tonsillectomy or the inhalation of a foreign body The right lung is more frequently involved than the left and the lower lobe more often than an upper lobe

*Etiology* —Abscess of the lung is usually caused by the aspiration of infected material or by an embolism from some distant focus In many cases, pathogenic organisms in the mouth or upper respiratory tract are aspirated during an operation particularly during tonsillectomy dental operations and nose and throat surgery Lung abscesses may also follow bronchial obstruction pneumococcic pneumonia subphrenic abscess an infected hydatid cyst bronchiectasis extension of esophageal malignancy bronchiogenic carcinoma and fungous infections of the lungs They may also follow injuries of the chest impaction of infected material conveyed by missles Both aerobic and anaerobic organisms are present in most cases

*Pathology* —A lung abscess begins in the pulmonary parenchyma usually distal to an occluded bronchus

been fully determined Penicillin has proved less successful against these abscesses than against nonputrid abscesses


REFERENCES

BATSON O V Function of the Vertebral Veins and Their Rôle in Spread of Metastases Ann Surg 1940 *115* 138

BURNETT W E Pulmonary Gangrene In NELSON W E Textbook of Pediatrics Philadelphia W B Saunders Co 1950

TOURHOFF A S W NABATOFF R A and NEUHOF H Acute Putrid Abscess of the Lung Late Results of Surgical Treatment J Thoracic Surg 1950 *20* 266

YOUNG R A and BEAUMONT G E Gangrene of the Lung In PRICE F W Textbook of the Practice of Medicine London Oxford University Press 8th ed 1950


## PULMONARY CYSTS

*Pathogenesis* —Cysts of the lung are of two types congenital and acquired Congenital cysts are distinguished by the muscle cartilage and bronchial glands found in their walls and by their epithelial lining Some contend however that cysts found without the epithelial lining may nevertheless be true congenital cysts that have lost that lining through infection and that acquired cysts may become epithelialized as a result of the opening established between the cyst and the bronchus Still the usual opinion is that the epithelial lining usually columnar and sometimes ciliated distinguishes the congenital from the acquired type of lung cyst Congenital lung cysts are generally found in children soon after birth or early in infancy The cysts may be filled with air or fluid or both Some such cysts are symptomless and are discovered later in life during routine radiologic examination Acquired lung cysts unless parasitic in origin develop after pulmonary infection or mechanical dysfunction

*Symptoms* —Marked respiratory symptoms at birth that do not respond to the usual resuscitation methods should suggest congenital lung cyst Radiologic examination may reveal a balloon cyst producing mediastinal and diaphragmatic displacement Fluoroscopy and serial films will aid in the diagnosis

Both children and adults with congenital lung cysts usually have had from birth episodes of cough dyspnea and cyanosis with or without episodes of respiratory infection such as bronchitis whooping-cough or pneumonia Ballooning cysts may cause a spontaneous or tension pneumothorax by rupture into the pleural cavity Recurrent respiratory episodes are common fever tachycardia and dyspnea indicating the presence of infectious processes

*In some instances radiologic examination* alone will suffice for diagnosis

*Treatment* —Usually no treatment is required If dyspnea is present or sepsis occurs as a result of infection surgical removal *of the cyst is indicated*

*Prognosis* —The cysts are more serious in childhood because of their tendency to balloon and cause respiratory dysfunction Rubin believes that once the patient reaches maturity without mishap the condition remains innocuous unless infection arises

*Mediastinal cysts* are usually congenital filled with liquid and found around the pulmonary hilus the trachea the cardiac area the esophagus and the pericardium They may be confused with thymic tumors aneurysms neurogenic tumors or other solid mediastinal tumors


REFERENCES

*Pulmonary Cysts*

ALLISON P R Giant Balloon Cysts of Lung Thorax 1947 2 169

GORDON BURGESS Pulmonary Cyst Dis Chest 1948 *14* 193

JOBIN J B Cysts of the Lung and of the Mediastinum Canad M J 1950 *63* 48

MOORMAN L J Cystic Disease of the Lungs In MYERS J A and MCKINLAY C A Chest and Heart Springfield Charles C Thomas 1948 v 1

POTTS W J and RIKER W L Differentiation of Congenital Cysts of the Lungs and Those Following Staphylococcic Pneumonia Arch Surg 1950 *61* 684


## TUBERCULOSIS

*Definition* —Tuberculosis is a widespread infective disease occurring in animals and man *It is caused by the tubercle bacillus* which may invade any part of the body, but usually invades the lung The disease

should be kept low to prevent aspiration into the trachea. When it is thought that a foreign body has been aspirated, bronchoscopic examination and removal of the foreign body, if found, follow at once.

Patients unconscious from alcohol, narcotics or trauma should have the head and neck kept low to prevent aspiration of infectious material. If an attack of pneumonia has not been properly resolved and there is wheezing or atelectasis, the patient should be examined bronchoscopically and any mucous plugs removed. These preventive measures, together with preoperative and postoperative use of antibiotics during internal surgery, should materially reduce the incidence of abscess of the lung.

## REFERENCES


BETTS, R. H.: Principles in the Management of Pulmonary Abscess. Am. J. Surg. 1941 54 82.

CHRISTIE, H. E., ARONOVITCH, M., and MEAKINS, J. F.: Aerosol Therapy for Lung Abscess. Canad. M. A. J. 1950 62 478.

EFSKIND, LEIF: Treatment of Primary Chronic Abscess of Lung. Acta Chir. Scand. 1950 99 391.

MYERS, J. A.: Pulmonary Abscess. In MYERS, J. A., and MCKINLAY, C. A.: Chest and Heart. Springfield, Charles C Thomas, v. 1, 1948.


## GANGRENE OF THE LUNG

*Definition.*—Gangrene of the lung (massive necrosis of the lung) and abscess of the lung are so closely related that it is difficult to distinguish sharply between them. But usually, pulmonary abscess is a localized lesion with rather sharp outlines and pulmonary gangrene a more diffuse condition without clear demarcation between the diseased and the healthy areas.

Gangrene of the lung, which usually affects one of the lower lung lobes, is a rapidly developing process characterized by massive destruction of pulmonary tissues, which become soft, pulpy and discolored. As the necrosis progresses, putrefactive liquefaction takes place; the fluid contains shreds of necrotic material and smells foul. The overlying pleura becomes intensely inflamed and the production of a putrid empyema or a pyopneumothorax is common.

*Etiology.*—Gangrenous suppuration of the lung may be a late sequel to bronchiectasis or a complication of bronchial obstruction caused by a tumor or a foreign body, or it may follow a lung hematoma arising from a severe contusion of the chest. Since Vincent's fusospirochetal organisms are frequently isolated from the necrotic tissue, some believe them of etiological significance. The general resistance of the body, the virulence of the invading organisms, and the degree of local vascular disturbance are all etiologic factors.

*Clinical Features.*—The most obvious features of gangrene of the lung are the extremely fetid breath and the putrid sputum, which often has a prune juice look. Hemorrhage is common and sometimes fatal. The symptoms are those of an acute toxic infection with remittent fever, chills, rapid pulse and prostration. Signs of an underlying disease such as bronchiectasis, aneurysm, or malignancy may also be present. The radiologic findings are suggestive of pneumonia, pulmonary abscess or, if the pleura is also involved, pleural effusion. Complications are uncommon because of the rapid progress of the disease.

*Complications.*—The usual complications of a gangrenous abscess are the spreading of the process into the pleura or the opposite lung and fatal hemorrhage. Occasionally an abscess of the brain may result from the lodgment of a septic embolus from the abscess. Such metastasis is made possible by the collateral circulation existing between the thoracic veins, the abdominal wall and the vertebral column, as described by Batson. The vertebral veins communicate with the intercostal veins, the abdominal veins and the azygos venous system. During cough the pressure in the pulmonary venous system is sufficient to send the blood into the collateral system.

*Treatment and Prognosis.*—The prognosis is generally poor. Only on rare occasions is the process subacute and chronic. Death may occur from one to three weeks after onset of the condition, particularly if the disease is apical.

*The only hope of cure, if the gangrenous process is not diffuse, lies in excision of the diseased area of the lung.* The role of the antimicrobial drugs in the treatment of gangrenous abscesses of the lung has not

until the patient becomes symptomless and the lungs radiologically clear. Streptomycin is indicated in all cases where symptoms seem to indicate a miliary tuberculosis without waiting for confirmation by discovery of tubercle bacilli in the sputum, for while the streptomycin is holding back the advance of the disease the general resistance of the patient can be built up for further protection. Many patients so treated tend to relapse as the organisms become resistant to the drug and in these death ensues.

The prognosis must be guarded. In some instances the disease is steadily progressive and fatal, the generalized tubercle formation causing an overwhelming toxicity. Use of the antibiotics in early cases may bring complete recovery. Continued therapy is indicated, since meningitis may develop many months after apparent recovery following streptomycin therapy.

*Acute pulmonary tuberculosis*, lobar or lobular in distribution, shows symptoms from onset, occurring in an apparently healthy person, and may be either caseous pneumonic or caseous bronchopneumonic in type. The onset and course of the infection resemble those of the pneumonias. *Acute lobar pneumonic tuberculosis* is an exudative process with symptoms resembling lobar pneumonia at onset. The rusty sputum and leucocytosis of the pneumonia, however, are usually absent and there is a greater remission of temperature than in pneumonia and there may be a slight hemoptysis. The



Fig. 152.—Miliary tuberculosis.

Administration as soon as the diagnosis is made of daily doses of streptomycin 2.0 Gm. intramuscularly is advocated for a period of from 4 to 6 months combined with complete bed rest. Others advocate administration of the drug for from 4 to 12 months with the addition of para-amino-salicylic acid to delay development of streptomycin resistance. Vitamin supplements and blood transfusion and other supportive measures should be used.

rarely absorbed or completely replaced by connective tissue, they may be held responsible for the chronic relapsing nature of tuberculosis. Nature tends to promote healing by segregating these foci from the adjoining tissues; to do this she produces a fibrous capsule with subsequent calcification. Whether the infection heals in this manner or progresses, breaks down, and leads to dissemination depends on the completeness of the immobilization of the tubercle bacilli.*

## CLINICAL FORMS OF PULMONARY TUBERCULOSIS

It is not always possible to classify a case of pulmonary tuberculosis as a particular type of the disease, but a number of general clinical forms may be recognized depending upon the extent, duration, accompanying symptoms, and particularly the pathogenesis of the lesion. The various ways in which reactivation of the primary process takes place has been described. The particular way in which this comes about determines the clinical form of the disease. When rupture into a blood vessel occurs with dissemination of foci throughout the lung, miliary tuberculosis develops. Rapid caseation, necrosis, and cavitation followed by rupture into a bronchus produce an acute pulmonary tuberculosis. A slowly advancing caseation of the process with continued infection leads to a chronic ulcerative tuberculosis, whereas a gradual transformation of a lobe or entire lung into a fibrous mass brings about a fibrotic tuberculosis.

*Miliary tuberculosis* results from a seeding of tubercle bacilli carried from an eroding caseous focus by the blood or the lymph to various parts of the body. In areas supplied with small capillaries the bacilli are filtered out and nodules form. Pancreas, stomach, thyroid, and brain are the least often affected. However, any organ or serous membrane may be infiltrated, but the lesions may be confined to one or both lungs or to one segment of one lung. The nodules, about 1 to 3 mm. in size, are found distributed within the parenchyma of the lung from apex to base, the tissues in between usually remaining clear of infection.

The disease arises most frequently in early childhood but may occur at any age. It is a complication of a small number of massive primary infections, usually developing within two years of their initiation. Miliary tuberculosis occurs not infrequently as a complication of a reinfection tuberculosis arising from a focus disseminating caseous material and spilling it into the blood stream. Myers states that it develops in approximately 1 per cent of all cases of chronic pulmonary tuberculosis. With further use of antibiotic therapy, miliary tuberculosis may occur less often.

In children, if the infection follows a primary lesion, the onset may be sudden with high fever, aching of the muscles, backache, and prostration. In adults the onset may be gradual with few symptoms, such as weakness and malaise, or no symptoms at all. In some cases even just before death x-ray evidence may be entirely lacking, but the diagnosis at this time may be suspected by positive ophthalmoscopic visualization of retinal tubercles and the recovery of tubercle bacilli from bone marrow aspiration. Early symptoms may be a gradual loss of weight and a persistent low grade fever; cough, if present, is mild and unproductive until the infection is well developed and then may be dry and irritating. These symptoms with enlargement of the spleen and distention of the abdomen may suggest typhoid fever, or the clinical manifestations may resemble those of bacterial endocarditis, sarcoidosis, or mycotic infections. The white-blood cell count may indicate a leukopenia or a leukocytosis, or if there should be a bone marrow involvement, a leukemoid reaction. Other symptoms noted may be due to the site of the infection or to the complications present in the affected organ.

Streptomycin therapy has been used successfully in checking the progress of the disease. Within a few days fever and toxicity may be abated and regression of the lesions may begin in a few weeks. In some instances this regression has continued

* National Tuberculosis Association 1950.

until the patient becomes symptomless and the lungs radiologically clear. Streptomycin is *indicated in all cases where symptoms* seem to indicate a miliary tuberculosis without waiting for confirmation by discovery of tubercle bacilli in the sputum, for while the streptomycin is holding back the advance *of the disease the general resistance of the* patient can be built up for further protection. Many patients so treated tend to relapse as the organisms become resistant to the drug and in these death ensues.

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disease is progressive in character, with rapid loss of weight prostration, and early death Caseation and necrosis occur rapidly but tubercle bacilli rarely appear until after the tenth day If fibrosis should occur, the patient may recover *Acute bronchopneumonic tuberculosis* is a lobular form of acute tuberculosis occurring chiefly in children and young persons with sudden onset and symptoms of an acute bronchopneumonia The lesions are widespread, involving an entire lung or portions of both lungs Extensive cavitation and caseation occur, but the lesions are usually small, due to short duration An initial dry cough becomes productive of copious purulent sputum the fever rises (with daily remissions) and the patient may become prostrate and cyanotic and die within a few days or weeks In these acute forms the inflammation is exudative in type Sometimes, in the untreated case recovery does occur after 6 or 8 weeks with resorption of the exudative elements and replacement by a fibrotic or productive process The case then becomes chronic

*Chronic productive tuberculosis* is of two forms, chronic ulcerative tuberculosis and chronic fibrotic tuberculosis Extension of the inflammatory process may be followed by periods of apparent stability The chronic forms of the disease are proliferative in character rather than exudative as in acute pulmonary tuberculosis, with a gradual development of fibrous tissue Destruction and repair may be taking place simultaneously in the affected lung Usually the infective process occurs at or near the apex of the lung it may extend to other parts of the lung to form a chronic ulcerative tuberculosis with cavity formation or undergo healing with formation of fibrous tissue, leading to chronic fibroid tuberculosis *Chronic ulcerative tuberculosis* or fibro ulcerative tuberculosis is characterized by repeated formation of areas of ulceration necrosis, and cavitation as periodic break downs in resistance occur This form of the disease is the most common and usually occurs in persons between the ages of 30 and 60 The onset may be insidious or may be sudden with severe symptoms which later subside leaving the patient incapacitated Signs of an exudative localized lesion with consolidation may be observed Cavitation and caseation are indicated by profuse purulent, and bacilli laden expectoration, hectic fever, night sweats, and hemoptysis In some cases, the inflammatory reaction is localized in the area of the initial infection the tubercle walled off by a fibrous wall These nodules may be quiescent until the caseous material breaks through the wall as necrosis develops liberating tubercle bacilli which produce other nodules in ad adjoining areas With each recurrence the lesion becomes more extensive with formation of local lesions which coalesce to form larger ones If the cavities are small, the fused areas may be converted into a dense fibrotic scar If a cavity is large, it may remain partially open but the partially occluded cavity may become imbedded in dense indurated tissue which confines the disease to a compact area permitting the patient to remain apparently well for a number of years However necrosis may occur and again liberate the enclosed tubercle bacilli *Chronic fibrotic tuberculosis* may follow an exudative process Healing may follow formation of the fibrotic tissues but ulcerative and fibrotic tuberculosis may coexist in various stages of healing The fibrotic tuberculosis may exist for years before symptoms are noted Fibrosis usually occurs when the disease is of long duration and is the type generally observed in patients over 50 The duration of the process not the age of the patient is the principal factor When the fibrosis is of considerable extent, permanent shrinking may occur in the lung, with displacement of the heart and mediastinum and retraction of the chest wall There may be a compensatory emphysema in the less affected lung In these cases tubercle bacilli may be scanty or absent from the sputum for long periods of time Various degrees of bronchiectasis may be present and these are hard to distinguish from small tuberculous cavities

## CLASSIFICATION

The classification adopted by the National Tuberculosis Association, seems the most acceptable ' By primary tuberculosis is meant those morbid processes which

follow directly and uninterruptedly the first implantation of tubercle bacilli

"Reinfection tuberculosis is a new infection in a person in whom a primary infection has been healed It is not always possible to determine, even at autopsy whether the infection is a primary one or a reinfection Extension of infection from a reactivated primary lesion may be thought of as an exacerbation of the process not a reinfection

culture or animal inoculation When sputum specimens are unobtainable or inadequate or their authenticity is in doubt examination by culture or animal inoculation should be made of fasting gastric washings or aspirated pulmonary secretions The period of inactivity must have existed for at least 6 months and should be indicated according to length of time, as inactive 6 months inactive 2 years' *etc*

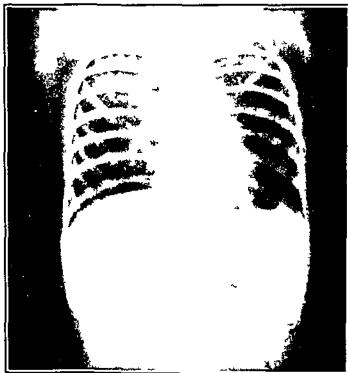


FIG 153 —Primary pulmonary tubercular infection arrested

A clinical classification is proposed in *Diagnostic Standards* to indicate (*a*) the status of the activity of the lesions according to symptomatic laboratory and roentgenologic findings (inactive arrested active or activity undetermined) and (*b*) the status of the patient in terms of exercise (not ambulatory ambulatory *etc*)

*Inactive* lesions are those in which there is *x* ray evidence of stability or extremely slow shrinkage and no *x* ray evidence of any cavitation Furthermore there are no symptoms of tuberculous activity and the sputum tests are repeatedly negative on concentration and microscopic study and on

For *arrested* lesions the symptomatic and roentgenologic requirements are the same as for inactive lesions, but the laboratory requirements are different When sputum specimens or gastric contents have proved negative on microscopic examination of concentrates but not of cultures or animal inoculations the lesions are considered arrested Arrested cases also include those in which culture or animal inoculation proves to be positive and among many concentrated specimens of sputum examined an occasional positive is found microscopically The period of arrest must have existed for at least 3 months and should be indicated

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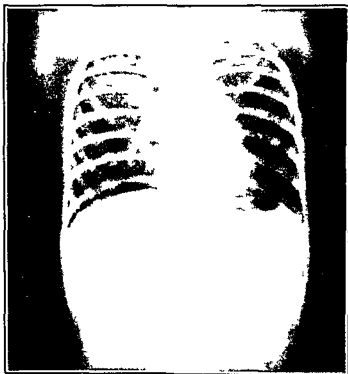


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according to length of time as "arrested 6 months," "arrested 2 years," *etc* *

*Active* lesions are those usually showing radiographic evidence of progression or retrogression although, occasionally, some are stationary. Clinical evidence of tuberculous origin may be present or absent. Almost always the sputum and gastric contents contain tubercle bacilli but occasionally repeated cultures and animal inoculations may fail to reveal bacilli. Very rarely the tuberculin test is negative. The period of activity if known should be indicated as "active 5 months," "active 2 years," *etc*

*Activity undetermined* applies to lesions whose activity cannot be determined even after adequate laboratory and roentgenologic studies. The provisional status may be indicated by "probably active" or "probably inactive."

The exercise status of the patient should be designated as follows: (I) Patient is not ambulatory; (II) patient has been ambulatory for less than one hour daily; (III) patient has been ambulatory for one hour daily for a period of 2 months; (IV) patient has been ambulatory for at least two hours daily for a period of at least 2 months; (V) patient is living under ordinary conditions of life. A patient therefore may be designated "inactive (6 months) III," *etc*



FIG 154 —Pulmonary tuberculosis minimal

A further classification is well defined in *Diagnostic Standards* to indicate the extent of pulmonary lesions. Thus the patient may have pulmonary tuberculosis that is minimal, moderately advanced or far advanced.

*Minimal* lesions are slight infections (without demonstrable excavation) confined to a small part of one or both lungs. Regardless of distribution the total extent of lesions shall not exceed the equivalent of the volume of lung tissue which lies above the second chondro-sternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side.

* There is not entire agreement on use of the classification "arrested." Salkin prefers use of a term which indicates an approach to inactivity such as "improved" or "quiescent." (Am Rev Tuberc 1951 *63* 721) Steele prefers to call this group "apparently inactive" and limited to patients whose pulmonary secretions are negative on concentration and have not been cultured because of lack of facilities. The Wisconsin State Board of Health omits the term "arrested" and calls all lesions active or inactive. (*Ibid* p 117)

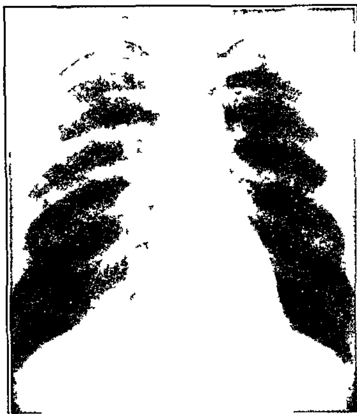


Fig 155 —Moderately advanced pulmonary tuberculosis



Fig 156 —Far advanced pulmonary tuberculosis

*Moderately advanced* lesions may involve one or both lungs but shall not exceed the following limits (1) slight disseminated lesions which may extend through not more than the volume of one lung or the equivalent in both lungs, (2) dense and confluent lesions which may extend through not more than the equivalent of one third of the volume of one lung, (3) total diameter of cavities less than 4 cm '

*Far advanced* lesions are those more extensive than moderately advanced A further suggestion is made that the location of lesions be designated by bronchopulmonary segments and the segments classified according to the recommendations of the American Association for Thoracic Surgery

BRONCHOPULMONARY SEGMENTS

| RIGHT LUNG | | LEFT LUNG | |
|---|---|---|---|
| LOBES | SEGMENTS | LOBES | SEGMENTS |
| | | *Upper* | |
| *Upper* | Apical | Upper Division | Apical posterior |
| | Posterior | | Anterior |
| | Anterior | Lower (Lingular) Division | Superior |
| *Middle* | Lateral | | Inferior |
| | Medial | | |
| *Lower* | Superior | *Lower* | Superior |
| | Medial Basal | | Anterior medial Basal |
| | Anterior Basal | | Lateral Basal |
| | Lateral Basal | | Posterior Basal |
| | Posterior Basal | | |

## CLINICAL MANIFESTATIONS

The symptoms and signs of tuberculous disease are not pathognomonic since they are similar to those of many other types of pulmonary infection In many instances the initial infection begins with a small area of exudative bronchopneumonia which enlarges very slowly over a period of months the patient may remain symptomless for a considerable time When symptoms finally occur and the patient is first brought under observation the disease may be far advanced beyond the stage when treatment is most effective Even in advanced cases the symptoms may be mild This emphasizes the need for early case finding and the values of mass *x* ray studies

The onset may be relatively sudden following what seems to be a bad cold or an attack of influenza which becomes progressively worse This may occur soon after the primary infection or develop many years after the disease has existed and the original focus has become calcified

*Fever* is one of the commonest manifestations of tuberculosis *it may be constant or* intermittent In minimal cases, a slight elevation of temperature may be observed in the late afternoon sometimes it is a rise of only half a degree in 24 hours As the disease progresses, the temperature may attain high levels, remaining unchanged for a number of weeks or months, then suddenly subside, only to reappear in a grippe like episode Even with a temperature of 102° or 103° F , the patient may remain comfortable except for a feeling of warmth and flushing of the face The fever may be accompanied by drenching sweats particularly at night

*Cough* is one of the most constant signs at first being non productive It is noted in over 50 per cent of the patients and at first may occur only in the morning in an effort to discharge accumulations of fluid in the bronchi but it becomes increasingly distressing with difficulty in raising these exudates Occasionally the cough is of neurotic origin and can be controlled

*Expectoration* a common symptom rarely occurs *in early or minimal pulmonary* tuberculosis At first the sputum may be small in amount about 1 oz daily and consist of only clear mucus Later with the

development of cavitation, 2 or 3 oz of a caseous colorless material which with progress of the disease becomes copious and yellowish green may be discharged daily A sudden increase in the amount of sputum may indicate that a recently formed lesion has penetrated a bronchus or that a bronchopleural fistula has formed On the other hand sudden decrease in the amount of sputum may indicate bronchial obstruction The sputum becomes foul only when a secondary infection by anaerobes has taken place

*Hemoptysis* may occur as only a faint streaking of blood in the sputum, or as a hemorrhage of a dram or more of blood It may be one of the earliest symptoms or may never occur at all The bleeding usually arises from ulceration of a blood vessel in a cavity or acute congestion around the lesion Usually the hemorrhage does not exceed 300 cc of blood and is followed by clotting which seals the opening Clots may be coughed up for several days or may be retained thus causing blocking of a bronchus and collapse of a lobe The hemorrhage may occur suddenly often during sleep at night and occasionally may be so massive as to cause drowning of the patient

*Hoarseness*, intermittent or persisting may indicate tuberculous lesions of the larynx or may merely be the result of incessant coughing *Wheezing* follows bronchial obstruction caused by mucous collections

*Dyspnea* on exertion in the early stage may accompany weakness or toxemia It may be continuous in advanced cases because of fibrotic changes in the lungs or may indicate serious myocardial weakness It may occur suddenly following spontaneous pneumothorax or may result from a rapidly accumulating pleural effusion

*Pain in the chest* aggravated by respiratory effort is a common symptom and an evidence of pleuritic involvement It may occur in any stage of the disease

Other symptoms occasionally observed include headache when the temperature is elevated increased pulse rate in the presence of toxemia and either increased or decreased digestive activity, according to the amount of toxemia present Constipation may be caused by the inactive life of the patient

These varied symptoms rarely if ever, all occur in one individual Some patients manifest few symptoms even in far advanced disease Furthermore most of these symptoms are observed in various combinations in other diseases of the lung and for this reason cannot be regarded as highly significant Only when considered together with the history of the patient and the laboratory and radiologic evidence are they important in making the diagnosis

Physical signs are also frequently minimal and not specifically characteristic However they should be observed to give a clear picture of the condition These signs may be absent in advanced cases with cavitation but, on the other hand they may be manifested in healed cases in which there are complications such as emphysema or bronchiectasis Palpation will reveal any displacement of the trachea or heart due to retraction of the lung caused by fibrosis or atelectasis Impairment of the percussion note at the apex of the lung is an early and reliable physical sign It may be noted long before development of gross consolidation of the lung and is generally more marked in the supraspinous fossa than below the clavicle Dullness on both sides may be noted if there is infiltration of the upper portions of the lungs this will increase in extent as consolidation progresses If a large cavity is present and not entirely filled with secretion, percussion over its site may produce resonance and tympany

*Auscultatory findings* will be dependent upon the location of the infection its closeness to the periphery of the lung and the amount of consolidation and cavitation Breath sounds may vary from bronchovesicular to bronchial breathing depending upon the extent of normal tissues between the affected regions Rales if present may be either fine or coarse depending upon the size of the bronchial ramifications and the secretion therein On slight cough at the end of a forced expiration followed by slow deep inspiration rales may be noted both during coughing and at the end of inspiration

Clubbing of the fingers except in old fibrotic cases will not be noted unless there is concurrent heart disease empyema, or bronchiectasis

## DIAGNOSIS

The *history* of the patient is of great importance in making a diagnosis of pulmonary tuberculosis Information regarding past respiratory illnesses, particularly a history of pleurisy with effusion, known tuberculosis in the family or other contacts, or employment in certain types of industry is of value in arriving at a diagnosis In the majority of cases, the contact is not known The final diagnosis is based upon the history, the symptoms physical examination, and the results of special studies especially sputum examination and $x$ ray of the chest

*Sputum examination* demonstrating the presence of tubercle bacilli is conclusive evidence of the disease A negative finding however cannot without other confirmation be considered proof of the absence of tuberculosis Sputum examinations must be conducted with great care The sputum must be collected over a 24 hour period its volume measured its consistency noted and tubercle bacilli searched for in smears stained (preferably) by the Ziehl Neelsen technique Concentrated sputum specimens should be examined when the bacilli are not demonstrated When there is little expectoration the specimen may be collected over a 24- to 72 hour period Two processes in preparation of the concentrated sputum are used (1) homogenization or emulsion and (2) concentration by gravity centrifugalization or separation When direct-smear and concentrated sputum studies are negative for tubercle bacilli but clinical evidence points to a tuberculous infection culture on desirable media or guinea pig inoculation are indicated If no sputum can be obtained the fasting gastric contents should be examined for bacilli

Sputum or gastric contents should never be considered negative for tubercle bacilli until at least three satisfactory specimens taken at least one week apart are negative by culture or by animal inoculation Finding one sputum specimen negative does not give assurance that another specimen will not reveal the presence of tubercle bacilli

*Gastric contents* collected on awakening may prove of value in demonstrating the presence of bacilli in children who swallow their sputum or in patients from whom sputum cannot be obtained This has proved an effective method of obtaining bacterial evidence but smears of gastric washings are unreliable because of the presence of other acid fast bacteria The washings therefore, must be cultured or inoculated into guinea pigs A series of negative examinations of sputum and/or gastric washings in the presence of cavitation may be considered evidence of the nonexistence of a tuberculous process

*Laryngeal swabs* on culture may be helpful but cannot be relied upon if no acid fast organisms are found

*Bronchial lavage* whereby 20 cc of warm saline solution are introduced into the bronchial tree and the expectorant then examined for acid fast organisms is favored by some clinicians There may be hazard of bronchial dissemination in this procedure

*Blood Changes* —During acute exacerbations, the polymorphonuclear leukocyte count may rise as high as 10 000 to 18 000 the neutrophils rising up to 80 per cent In early acute active tuberculous pneumonia and in acute miliary tuberculosis the white cell count may be elevated to more than 20 000 and the polymorphonuclear count to over 95 per cent In chronic cases, the white cell count tends to remain normal The neutrophils increase with the progress of the disease decrease in their number usually accompanies general improvement However the lymphocyte monocyte *ratio* is of limited value since this may be altered by intercurrent infections

The erythrocyte count and the hemoglobin content generally remain normal in chronic cases but may decrease in active and acute cases until a mild anemia is observed This anemia does not become marked even in far advanced cases unless extrapulmonary complications are present

The sedimentation rate may remain normal in minimal tuberculous disease but is usually elevated in the advanced febrile stages A normal sedimentation rate does

not signify inactivity or favorable progress of the disease since it may be found normal both in early active cases and in chronic cases

*Urine examination* may reveal the presence of tubercle bacilli in patients with renal tuberculosis There may be no other urinary abnormalities Finding these bacilli in the urine should initiate search for pulmonary tuberculosis if it is not already known to be present On the other hand pus cells a persistently marked increase in the number of erythrocytes or persistent albuminuria in the urine of a patient with pulmonary tuberculosis should lead to a search for the renal tuberculosis

The *tuberculin test* is a valuable means of revealing tuberculous infection A positive reaction always indicates the presence of such a process, but gives no information regarding the activity of the disease, the test indicating only that at some period in his life the patient has been infected with tubercle bacilli When no reaction is elicited after repeated doses of tuberculin it is generally assumed that no infection is present However the dosage may have been too small to indicate infection in well-healed lesions or an acute infectious disease may also have been present such as measles or influenza Whenever there is a suspicion of a tuberculous process the test should be used In persons with long-standing lesions only large doses may produce a reaction

The intracutaneous Mantoux test or the Vollmer patch test may be used For routine case finding the Mantoux method is generally preferred Either 0 1 mg of old Tuberculin (OT) or purified protein derivative (PPD) with first or second strength test dose is injected into the superficial layer of skin In very ill patients the initial concentration should be only 0 01 mg of OT or 0 00001 mg of PPD A reddened wheal with induration and edema of the subcutaneous tissues may be observed 72 to 96 hours after the test in positive cases Any redness due to trauma will have faded by that time The degree of redness is not significant but the reaction may be intense in recent infections or reinfections If negative results are obtained the test should be repeated after 4 or 5 days with a higher concentration of the testing material No reaction will be noted in the pre allergic stage (3 to 7 weeks after the primary infection), nor during the terminal stage, when the pulmonary tissues are desensitized (anergic phase)

The Vollmer patch method consists of application to the skin for a 48 hour period of a piece of gauze impregnated with dried tuberculin After 72 to 96 hours a red papular, sometimes vesicular eruption may be noted in positive cases This method is often preferred in children

The significance of a positive tuberculin test varies with the age of the individual A positive test in children under 2 years of age may indicate the presence of an active lesion unless radiologic findings examination of the gastric contents and careful observation prove otherwise Active disease is not necessarily indicated by a positive test in young children although the younger the child the more likely the lesion is to be active especially if there is a history of recent contact A reactor should be retested every 3 to 5 years to determine whether the infection has disappeared

Certain limitations in tuberculin skin testing should be noted First a negative test should be repeated within 6 weeks if the contact has been recent since hypersensitivity may not yet have been developed Second not infrequently a negative finding is obtained in cases of far advanced generalized or meningeal tuberculosis in moribund patients and in the presence of acute infectious diseases such as measles and scarlet fever Third allergic manifestations may cease in patients with calcified foci representing completely healed earlier lesions Finally it has been demonstrated that a small percentage of clinically tuberculous patients although in a very advanced stage of the disease may yield a negative reaction for this reason when clinical evidence strongly favors a diagnosis of tuberculosis a negative test may not be clinically significant

*Bone marrow examinations* may reveal the presence of bacilli in cases of hematogenous tuberculosis The process whereby these bacilli reach the bone marrow has

not been determined—whether tubercle bacilli extending from a caseous focus through the lymphatics reach the thoracic duct and then enter the circulation, whether direct extension of a caseous lymph node into a vein forms a tubercle within the vein for hematogenous seeding, whether caseous foci are a disseminating source or whether tubercle bacilli drain from an active extrapulmonary focus to the regional caseous lymphnode and then, by way of the lymphohematogenous route, finally reach the circulation is not known No one mechanism may be responsible and any one or a combination of two or more of these processes may cause invasion of the blood stream When hematogenous dissemination is present without pulmonary lesions, then *x* ray study and bacteriologic examination of the sputum and gastric washings are valueless However, in many cases, the lung ultimately becomes involved Katz noted that in three-quarters of his hematogenous cases, bone marrow studies were positive on the first examination but the test cannot be considered negative until three aspirations have been made The bone marrow may contain tubercle bacilli even before they can be identified in the sputum, the gastric washings, the lymph nodes or the spinal fluid Since it has been demonstrated that early administration of streptomycin may inhibit or arrest a tuberculous process and since a bone marrow examination may reveal the presence of the disease before localization has occurred bone marrow examination may also indicate the effectiveness of streptomycin therapy After the disease becomes quiescent the bone marrow may still remain positive an indication *that the bacilli have remained resistant to* streptomycin and that further use of the drug may be without value

*X ray examinations* are indicated in all suspicious cases of pulmonary infection When a large group of apparently healthy individuals are studied roentgenologically most of those found to have pulmonary tuberculosis have minimal lesions Of those who report to physicians because of pulmonary symptoms a majority will show evidence of moderately or far advanced tuberculous processes Some having negative roentgenograms one year later may show shadows indicating moderately or well advanced tuberculous lesions Chronic tuberculosis may have existed for a considerable period yet show no evidence of advancement, so that it cannot be determined when the infection first occurred

Except for tubercle bacilli tests, roentgen examination furnishes the most conclusive evidence of the disease It also indicates how effective therapeutic measures are whether there has been healing of reinfective parenchymal tuberculosis and whether any cavitation, fibrosis or calcification is present

Fluoroscopic study of the lungs though inadequate for detecting early tuberculous lesions, is helpful in defining the position, the contour, and the movement of the cardiac and diaphragmatic shadows and in showing the mediastinal areas These cannot be determined by routine *x* rays of the chest Photo fluorograms of these images can be made on small films and enlarged for study However since fluoroscopy fails to reveal from 10 to 15 per cent of the minimal lesions it cannot be substituted for radiography

Certain limitations in roentgenologic diagnosis have been noted First the usual *x* ray film will show only 75 per cent of the lung because of shadows of the heart and diaphragm Second though numerous lesions may exist within the field *x* rayed they may not cast perceptible shadows either because they are too small to do so or because they are not of the necessary consistency to absorb *x* rays Third an accurate diagnosis of the pulmonary lesions cannot be made from their shadows alone since many of these shadows are observed *in other pulmonary* diseases Fourth neither progression nor retrogression of the tuberculous process can be determined unless new films are taken periodically Finally the location of pulmonary lesions casting shadows cannot be regarded as a satisfactory diagnostic criterion Though chronic tuberculosis usually occurs in the upper part of the lung it often develops first in the lower part Furthermore though nontuberculous conditions usually appear in the lower part of the lung they sometimes occur in the upper part

*Differential Diagnosis*.—Most of the radiologic findings in pulmonary tuberculosis are also observed in such nontuberculous conditions as diseases of the lymph glands and blood vessels, bronchial disorders, inflammatory parenchymal lesions, neoplasms, pleural lesions, and many other pulmonary affections, including those secondary to cardiovascular disturbances.

*Upper respiratory infections*, such as sinusitis, tonsilitis, bronchitis, influenza and protracted colds, may simulate pulmonary tuberculosis, particularly with respect to the stubborn or recurrent cough. Frequently, adequate treatment of the paranasal sinuses and removal of infected tonsils will cause the symptoms to disappear. Examination of the sputum will fail to show tubercle bacilli.

*Chronic bronchitis* frequently suggests tuberculosis. The cough may be strenuous and dry, or productive of small quantities of viscid mucoid sputum or large quantities of mucopurulent and occasionally blood-tinged sputum, depending upon the underlying cause. No persistent cough, however, should be considered indicative of chronic bronchitis unless tuberculosis has been carefully ruled out. X-ray examination in cases of bronchitis may reveal thickened hilum shadows, markedly increased bronchovascular linear markings, particularly toward the bases, and evidence of emphysema.

*Bronchiectasis* commonly reveals symptoms resembling those of tuberculosis. Chills, fever and sweating, however, occur more persistently in tuberculosis. Bronchiectasis may be suspected when the lesion is situated in the lower lobe, although it occasionally also occurs in the upper lobe. The roentgenogram may be normal or show increased linear densities extending downward from the hilar areas. If bronchiectasis is suspected, failure to find acid-fast organisms should rule out tuberculosis. But the two diseases may exist concurrently. *Pulmonary hemorrhage* which may occur with either disease sometimes leads to an erroneous diagnosis.

The *pneumonias*, except for a frank lobar pneumonia, may be confused with tuberculosis, and a tuberculous pneumonia is easily confused with an acute pneumonia; only when it fails to respond to drug therapy is the error recognized.

Primary atypical pneumonia may present clinical and radiologic pictures similar to those of tuberculosis, but in the former the absence of cavitation, the absence of tubercle bacilli in the sputum, and eventual and complete resolution of the pulmonary lesion will establish the diagnosis.

Friedländer's pneumonia is chiefly distinguished from tuberculosis by the rapid spread of consolidation from one lobe to another and the copious expectoration of blood-tinged sputum of a mucinous, chocolate-pudding nature. Examination of the sputum will usually establish the diagnosis.

Bronchopneumonia is distinguished from early tuberculosis by its acute onset and rapid abatement of symptoms.

Lipoid pneumonia is differentiated from tuberculosis by demonstration of oil droplets in the sputum. Usually a history of the use of oily medications can be obtained from patients with lipoid pneumonia.

The response to penicillin therapy distinguishes all types of pneumonia from tuberculosis, since the drug has no effect upon the latter disease.

*Loeffler's syndrome*, except for the variability of the roentgenologic findings which may be transitory and migratory, may be mistaken for tuberculosis. Fatigue, malaise, cough sometimes associated with chest pain and productive of a small amount of sputum, mild asthmatic attacks, bronchitis, and some elevation of temperature should suggest the former disease. The blood picture shows a fairly high leukocytosis, somewhat elevated sedimentation rate and a high eosinophile count. Diagnosis depends upon serial roentgenologic observations and blood and sputum studies.

*Abscess of the lung* is often difficult to distinguish from a tuberculous lesion radiologically; however, the abscess usually shows more precise outlines than the tuberculous lesion. The abscess may be obscured by exudation, atelectasis and pneumonitis; when visible it is a fairly dense homogenous round circumscribed or irregularly shaped shadow. When necrosis and empyema de-

velop, the lesion is again overshadowed Bronchoscopic examination will aid in the differential diagnosis Penicillin may be effective if the lesion is an abscess, if the lesion is tuberculous penicillin will not be effective Intensive search for tubercle bacilli should be made in all cases of suspected lung abscess

*Bronchiogenic carcinoma* with cough hemoptysis dyspnea fever chest pain, unilateral wheezing and weight loss is suggestive of tuberculosis especially in the middle aged The radiologic findings are often similar to those of tuberculosis

Bronchoscopy may permit direct view of the growth unless it is in the hilar area but in some cases will not reveal the growth until it bulges or breaks into a large bronchus The tumor may be indicated by a narrowed and distorted bronchial tree with congestion edema and obstruction Cytologic study of bronchial aspirations or a punch biopsy may reveal cancer cells but the latter is not generally recommended A biopsy of a superficial metastatic lesion in a lymph node may also be diagnostic Diagnostic thoracotomy and bronchography are other aids to diagnosis

*Hodgkin s Disease* — A study of the lymph nodes and skin lesions helps reveal the presence of Hodgkin s disease Tuberculosis which may exist concurrently is discovered by sputum examination

*Cardiovascular disturbances* may also suggest tuberculosis Hemoptysis frequently occurs in both mitral stenosis and hypertension Chronic pulmonary congestion may lead to pulmonary fibrosis and infected pulmonary infarcts may develop into abscesses simulating tuberculous cavitation Positive diagnosis rests upon the laboratory findings

*Pulmonary fibrosis and emphysema* may occur with or without chronic disseminated tuberculosis Chronic cough hemoptysis and increasing weakness may give rise to a suspicion of tuberculosis

*Sarcoidosis*, radiologically shows enlarged lymph nodes usually bilateral and symmetrical involving the peribronchial rather than the peritracheal nodes The extensive x ray changes are entirely out of proportion to the symptoms, for the patients often appear to be in excellent health If the cervical nodes are enlarged, biopsy may be required to distinguish sarcoidosis from tuberculosis

*Pneumoconioses*, of which silicosis siderosis, anthracosis and asbestosis are the most common types, are occupational diseases with few physical signs except in the presence of complications, but they give rise to conditions mimicking tuberculosis The marked dyspnea is in contrast to the general good condition However, there is little weight loss there is usually no fever and the fatigue is much less pronounced than in tuberculosis The radiologic appearance is similar to that of tuberculosis

Some of the pneumoconioses particularly silicosis seem to favor the development of tuberculosis When marked exudatione consolidation and cavitation are present, an associated tuberculosis should be suspected and tubercle bacilli searched for in the sputum

*Coccidioidomycosis* and other mycotic diseases causing densities cavitation and miliary spread may so closely resemble tuberculosis that only immunologic or bacterial study will distinguish them from tuberculosis

*Psittacosis* (ornithosis) may in mild cases be confused with pulmonary tuberculosis The disease can be diagnosed only by recovery of the causative virus from the sputum

## Complications

Pulmonary tuberculosis is not uncommonly complicated by tuberculous processes in other parts of the body Only rarely however does primary tuberculosis occur outside the lung when it does involvement of the lung is almost certain to follow Involvement of other organs may follow dissemination of the tubercle bacilli by way of the blood or the lymph or it may occur through spread of the infection to areas adjoining the lung

*Pleural involvement* is one of the most frequent complications of pulmonary tuberculosis especially in acute cases Pleural effusion in children is always serious and should arouse a suspicion of tuberculosis A patient may complain of pain in the chest

but fluoroscopic and roentgenologic examination may fail to reveal any evidence of pleural effusion until some time after the pain has subsided. Except in mild dry pleurisy, pain in tuberculous pleurisy is followed by slight fever, which increases as the pleural fluid develops, at which time the pain diminishes. The symptoms are those of any other pleural effusion. A positive diagnosis of tuberculous pleurisy is made only by laboratory studies of the fluid or by thoracoscopic examination. Some clinicians believe that thoracentesis is indicated only when examination of the fluid is desired and the effusion is so great as to make x-ray study impossible. Pneumothorax is not advised in simple tuberculous pleurisy, since it may lead to tuberculous empyema.

When the exudate of a tuberculous pleural infection becomes purulent, tuberculous empyema develops. Tuberculous empyema may develop spontaneously or as a complication of artificial pneumothorax. The fluid is thick and purulent and usually contains tubercle bacilli. If no fistula is present, Hayes advises repeated aspirations, pleural lavage with such disinfecting and detergent agents as azochloramide and tergitol, and maintenance of a negative intrapleural pressure. Aspirations and irrigations are usually ineffective in preventing further thickening of the fluid, and the empyema becomes chronic unless the lung can be reexpanded and the empyema quickly cleared up. If reexpansion does not occur, streptokinase may be tried; if not successful, decortication or thoracoplasty may be necessary. If a bronchopleural fistula develops, immediate intercostal drainage is required to prevent spread of infection to the opposite side. Streptomycin therapy, unsuccessful in closed treatment of tuberculous empyema, has proved valuable in local open treatment of the condition in conjunction with thoracoplasty or muscle implantation.

*Tuberculosis of the larynx* is a serious complication of pulmonary tuberculosis and usually indicates progressive disease.

Early cases may be asymptomatic. A hacking cough may develop because of tickling or scratching sensations or excessive dryness in the throat. Voice changes occur with vocal cord involvement, hence chronic hoarseness should suggest tuberculosis. Pain occurs only in advanced cases and increases with coughing. Ulcers may form on the vocal cords and give them a moth-eaten appearance, or the cords may become edematous. Severe laryngeal pain may be referred to the ear. Dyspnea caused by laryngeal obstruction rarely occurs. Dysphagia and odynophagia, when present, interfere with nutrition.

*Tuberculous tracheobronchitis* may result from direct extension of the infection or dissemination of the bacilli by the blood or the lymph. It is said to occur in approximately ten per cent of the cases of pulmonary tuberculosis and is a serious complication. If limited to the smaller bronchi in the vicinity of a caseating focus, it occasionally brings about collapse of the lung; on the other hand, it may distend a small cavity arising from the liquefied focus. The larger bronchi, even at some distance from the original focus, may become involved; if an incomplete obstruction results, emphysema will develop; if the obstruction is complete, atelectasis will follow.

Ulcerative tuberculous tracheobronchitis may cause the appearance of tubercle bacilli in the sputum in cases without x-ray evidence of pulmonary tuberculosis. The nonulcerative nonstenotic type is the most common. Wheezing, paroxysmal coughing and unexplained dyspnea are common symptoms. Gross obstruction of the bronchus rarely occurs but, when it does, gives a poor prognosis. In such a case persistent cough and difficult expectoration are noted, together with rhonchi at the site of obstruction that are loud enough to be heard without a stethoscope.

Treatment should attempt to reestablish and maintain bronchial drainage. For simple or tracheal ulcers, cauterization with 30 per cent silver nitrate solution or electrocauterization is recommended. Secretions should be aspirated repeatedly. Streptomycin therapy is advised in acute or subacute cases. Inhalation therapy and the use of atropine, adrenalin, ephedrine and vaccines have also been suggested.

The prognosis is dependent upon the degree of infection when the disease is

diagnosed. Small lesions with hyperemia may heal spontaneously. In patients with a severe degree of stenosis, Cohen finds that a mortality rate of from 25 to 35 per cent may be expected some 5 years after discovery of the tuberculous tracheobronchitis. Patients with a chronic condition, however, may survive for an indefinite period under proper care.

*Tuberculosis of the digestive tract* is now being seen with decreasing frequency. Hayes reports that the stomach was found to be involved in less than 1 per cent of several thousand autopsy cases of pulmonary tuberculosis. He suggests that some of the so-called tuberculous ulcers of the stomach may be peptic ulcers secondarily infected with tubercle bacilli. However, miliary tuberculosis is a known cause of tuberculous ulceration of the stomach. The treatment is usually medical, although the ulcer may be excised if the patient's condition permits.

Tuberculosis of the intestines occurs only after cavitation has taken place in a lung and usually results, it is believed, from the swallowing of sputum containing tubercle bacilli. Rubin found intestinal tuberculosis in 65 per cent of 526 patients dying of pulmonary tuberculosis. He noted that patients under 30 develop intestinal tuberculosis twice as often as those over 50 and that it occurs more often in females than in males, except between the ages of 21 and 30. Furthermore, intestinal tuberculosis occurs twice as often in patients with laryngeal tuberculosis as in those without laryngeal infection. Fluoroscopic and gastrointestinal studies are suggested for suspected cases. The most usual site of the infection is in the ileo-cecal region, the ileum being involved in 89 per cent of patients and the cecum in 75 per cent.

In intestinal tuberculosis, there may be no symptoms or such symptoms as colic, indigestion and diarrhea alternating with constipation. The severity of the symptoms does not depend on the amount of disease; small lesions may produce many symptoms while in some patients extensive disease causes few symptoms. Loss of weight or unexplained fever may be the only symptoms. Roentgen examination may reveal the Stierlin phenomenon, that is, nonfilling of the cecum and terminal ileum with barium and irritability of the rest of the ileum and colon. Mild pain may be aggravated by eating, and there may be slight fever in the evening and subnormal temperature in the morning. The lesion may heal with improvement of the pulmonary infection. Symptomatic therapy includes strict bed rest, use of a high caloric, low protein, smooth diet supplemented with cod liver oil, tomato juice, and vitamins. Hayes and Adams recommend oxyperitoneum in suspected cases of secondary intestinal involvement either as a therapeutic test or as a means of treatment. Usually oxygen from 300 to 500 cc is injected, this being given every 5 to 7 days until the acute symptoms subside. The effects may be observed immediately or in from 24 to 48 hours. Excellent results have been achieved with streptomycin therapy. The prognosis in patients with intestinal tuberculosis is good when diagnosed early and promptly and adequately treated. Recovery depends upon cure of the lung involvement.

Ischiorectal abscesses and fistula in ano are frequently observed in patients with perianal tuberculosis. These conditions may precede the appearance of clinical symptoms. The fistulous tract should be resected, care being taken to locate the internal opening. Healing may require months.

Tuberculous peritonitis may accompany tuberculosis of the fallopian tubes, tuberculous enteritis, tuberculosis of the mesenteric nodes, or miliary tuberculosis. It is usually insidious in onset and presents mild, vague symptoms. The disease has been successfully treated with injection of 300 to 500 cc of oxygen into the peritoneal cavity, repeated at weekly intervals if necessary. Five or six treatments may suffice in acute cases, but chronic cases may require continuance for a year. If effusion is present the fluid should be aspirated before injection. To date, results of therapy with streptomycin have been excellent.

*Tuberculosis of the genitourinary organs* has greatly decreased in the past two decades. (*See* page 1033.)

Genital tuberculosis is not frequently reported; it is primarily a disease of youth

If material can be expressed from the prostate gland tubercle bacilli may be found Tuberculous lesions of the testes are rarely observed except as an extension from the epididymis Infection of the epididymides is bilateral in half the cases and may cause swelling tenderness and contour changes with extension into the vas deferens The infection may be subacute and quiescent with only slight tenderness and swelling later however it may be activated by trauma and produce acute symptoms Involvement of the seminal vessels produces discomfort at the neck of the bladder and low back pain Treatment of the pulmonary and renal tuberculosis may arrest the glandular infection

Genital tuberculosis occurs half as frequently in females as in males and in the former it most often involves the fallopian tubes with secondary spread to the uterine endometrium and ovaries Radiation therapy has been found helpful except in case of marked fever toxemia or massive lesions Sanatorium care or enforced rest is necessary the period of time required varying with the patient Use of streptomycin therapy seems promising but it is in the experimental stage

*Pregnancy in tuberculous women* when adequate care is provided need have no unfavorable effect on the tuberculosis nor need tuberculosis adversely affect the pregnancy The pregnant patient may be unaware of her tuberculous condition although it may be well advanced The practice of prenatal care has led to more frequent discovery of the condition Determination of the activity of the lesion must be made at once and the woman placed under the care of a physician experienced in treatment of tuberculosis Close relationship between the chest specialist and the obstetrician has resulted in the present good results obtained in these patients Sanatorium care for the pregnant patient with active tuberculosis should be urged The patient with a stabilized lesion should be hospitalized for some time before the expected date of delivery

The treatment of the tuberculous pregnant woman is the same as for other tuberculous patients—bed rest antimicrobial agents collapse measures and surgical therapy if indicated

A normal child can be expected whether the mother s tuberculosis is inactive or active Chances of intrauterine infection of the child are slight Since the strain of childbirth and the wide excursions of the diaphragm during labor will nullify some of the benefits obtained from the long bed rest the second stage of labor should be made as short and easy as possible Rules regarding the choice of anesthetics are the same as for any other surgical procedures in tuberculosis Caesarian section is not indicated except for the usual obstetrical reasons

The newborn infant must be removed immediately from contact with the infected mother The only real danger to the tuberculous mother occurs not during the pregnancy but after delivery If the mother attempts to care for her baby, and in addition to perform household duties she is in danger of activating her disease if it has been inactive or of making it rapidly progressive if it is active

*Tuberculosis of the bones* may occur at any age but is found most often in children Except for the primary infection there may be no evidence of tuberculosis in the lung parenchyma however search should be made for tuberculous lesions in the kidney and genital areas Tuberculosis of the spine or hip may progress rapidly Usually the tubercle bacilli slowly invade a joint from a focus near the epiphysis and extend toward the peritoneum forming bony sequestra and abscesses and causing necrosis of the bony structures Hard coughing may cause fracture of a rib usually on the anterolateral aspect of the chest Radiologic evidence is presented only after atrophy destruction and condensation take place Finding of bacilli by biopsy or bacteriologic examination confirms the diagnosis Treatment consists of complete rest nutritious diet freedom from weight bearing and later fusion of the bones and resection of joints as indicated Adjuvant therapy includes heliotherapy ultraviolet radiation and administration of streptomycin with PAS

*Tuberculous meningitis* the pathogenesis of which has long been subject to controversy, may be the terminal stage of a hematogenous tuberculosis situated within the brain (the principal focus) the spinal cord the meninges themselves the choroid plexus, or a bone in the vicinity of the central nervous system It occurs most frequently in infants between the ages of 6 and 18 months, only seldom does it occur in children over 10 It is estimated that 60 per cent of all infants and children dying of tuberculosis have meningitis A persistent uncontrollable headache and rising temperature in children are suggestive of the disease The onset of the disease is insidious and the course is protracted occasionally with remissions Nausea and vomiting may be the only symptoms Fever occurs when the disease is well advanced It may be mistaken for encephalitis suppurative meningitis convulsive states or delirium Irritability, fretfulness and personality changes may occur in the adult

Diagnosis depends on the recovery of tubercle bacilli from spinal fluid The spinal fluid may show increased protein decreased chloride and sugar some lymphocytes and a great increase in the number of neutrophils Until the advent of streptomycin treatment was merely palliative Hayes and Adames report recovery in 50 per cent of their patients treated with parenteral and intrathecal injections of streptomycin 1 mg per kg body weight up to 50 mg dissolved in 10 cc of normal saline solution This is given once a day for several days then on alternate days and finally every third day for 90 days *Iglee* advocates giving streptomycin parenterally and intrathecally in all cases of tuberculous meningitis

*Tuberculous pyopneumothorax* due to perforation of a subpleural caseous focus is very serious and may lead to death When there is a large bronchopleural fistula, air enters the pleural cavity more quickly than it can be withdrawn this demands quick aspiration and treatment for shock An in-dwelling needle or some type of continuous suction under water is required to allow escape of the air A mixed infection often results and causes a stormy course Anoxemia may be relieved by oxygen therapy Thoracotomy and intercostal drainage are indicated and should be followed by thoracoplasty or pleuropneumonectomy as soon as the patient's condition permits The latter goal may be reached more effectively by relieving toxicity by means of appropriate antibiotic therapy and chemotherapy directed against the mixed infection

*Adenitis* occurring during reinfection tuberculosis can be successfully treated radiologically Cervical and mesenteric lymph node involvement is rare Tuberculous cervical adenopathy is generally associated with bovine strain and stems from ingestion of contaminated milk The diagnosis is established by biopsy tuberculin tests, or laboratory study of discharges from a sinus Conservative therapy with ultraviolet light or roentgen rays, should be employed before surgery, since many cases respond to such therapy alone When fluctuation, abscess formation or discharging sinus is present antimicrobial therapy may be employed in conjunction with surgery Incision and drainage of softened nodes or removal of solitary nodes may be necessary For tuberculous abscesses aspiration of the pus lavage of the cavity with a 1 per cent aqueous solution of tincture of iodine and injection of oxygen into the pocket are suggested PAS solution may also be employed in abscess cavities or sinuses

*Diabetes* in patients with pulmonary tuberculosis particularly severe or inadequately controlled diabetes is a serious complication Diabetes is usually the primary disease The incidence of tuberculosis among diabetics is substantially greater than it is among the general population These facts stress the necessity of periodic chest *x* rays for all diabetics In comparison with the nondiabetic the diabetic more often presents himself with far advanced tuberculous disease of an acute exudative or pneumonic nature with evidence of marked tissue destruction caseation and cavitation

Treatment requires control of the diabetes by diet and insulin and of the tuberculosis by collapse therapy or other indicated measures particularly antimicrobial therapy Kayne points out that tuberculous diabetics frequently have too low a diet since tuber

culosis requires liberal feeding the conflict may be managed by giving increased food and adjusting the insulin requirement

Successful treatment of several elderly patients by thoracoplasty has been reported by Rubin Collapse therapy should be induced immediately without waiting for the usual period of bed rest if the diabetes becomes uncontrollable or chest symptoms develop Improvement of either condition will benefit the other

*Bronchiectasis secondary to tuberculosis* a relatively frequent finding is often unrecognized However this bronchiectasis may be significant and overshadow the tuberculosis in importance since it may determine the development of the pulmonary lesion and the direction of management The course and prognosis of pulmonary tuberculosis may be adversely influenced by secondary bronchiectasis since (1) bronchiectatic suppuration may break down an encapsulated focus or interfere with repair (2) tuberculosis in the presence of bronchiectasis may be spread by purulent secretions and hemoptyses and (3) pulmonary symptoms due to bronchiectasis may persist despite negative sputum and apparently adequate treatment for pulmonary tuberculosis Moreover collapse treatment directed toward tuberculosis may be unsuccessful as a result of secondary bronchiectasis Therefore treatment of the bronchiectasis by pulmonary resection may assume primary importance

Bronchiectasis in the tuberculous patient should be suspected when productive cough low grade fever and occasional hemoptyses persist despite sputum conversion and apparent arrest of tuberculosis and when negative sputum persists in apparent clinical or radiologic cavitary tuberculosis It must be pointed out that bronchiectasis in the sputum negative tuberculous patient may resemble active tuberculosis

The pathogenic mechanisms of bronchiectasis secondary to tuberculosis are dependent upon a combination of bronchial and parenchymal factors Of many factors bronchial obstruction and reduction in volume of aerated lung (atelectasis) appear to be the most important Bronchial infection pneumonic consolidation and pulmonary fibrosis are secondary factors

## TUBERCULOSIS IN OLDER PATIENTS

Many tuberculous old people die without diagnosis of their tuberculosis the lesions have burned out The symptoms if they exist at all are only mild Yet these patients may infect other people No case finding campaign is complete if it neglects the aged These should receive special attention If the findings are negative reexaminations should be conducted regularly Old seemingly inactive fibrosed lesions may be only smoldering and though not progressive may be liberating tubercle bacilli without affecting the activity of the patient

Primary tuberculosis may occur in older persons but most cases of the tuberculosis in the old are benign or chronic

## TREATMENT OF TUBERCULOSIS

*Evaluation of the Tuberculous Lesion — To institutionalize an individual because of* the presence of an x ray shadow which represents a well-stabilized lesion is a serious error It is equally serious to withhold or delay treatment in a patient with a progressive process just because there is no radiologic evidence of activity Evaluation of the tuberculous lesion and the need for treatment therefore call for careful weighing of the evidence presented and decision as to whether the lesions are arrested or are still active and whether progressive or receding

Primary tuberculosis observed most often in children usually requires no treatment The tubercle bacilli allergy reaches its height in from 3 to 7 weeks In approximately 5 per cent of those infected for the first time radiologic evidence and clinical symptoms can be observed Accelerated erythrocyte sedimentation rate slight fever and malaise may be noted at this time but after bed rest these generally disappear If a dense homogenous focus with collateral inflammation is observed radiologically bronchoscopy may indicate whether this shadow results from an atelectasis caused by bronchial obstruction or from a primary focus A shadow cast by a primary focus may last for a few months without sympto-

matic manifestations then slowly resolve In a few children, a lesion may develop that is too small to observe radiologically, but it may later show calcified deposits If the shadow is due to atelectasis, streptomycin therapy is helpful and may prevent development of bronchiectasis, but if the shadow is evidence of a primary focus, unless this process is progressive streptomycin is of no value and might only cause development of streptomycin resistant bacilli and so prevent use of the drug against a subsequent serious tuberculous infection Most of the primary cases resolve spontaneously A child with a primary tuberculosis should be removed immediately from contact with the infecting person and have periodic *x* ray examinations to determine whether an active process has developed

Primary tuberculosis may occur in adults and tuberculous adults should be examined periodically to discover any reactivation or new infection as soon as possible since the success of therapy depends upon the duration of the infection its extent and the promptness with which treatment is initiated

Necropsy evidence and occasional clinical findings show that approximately 25 per cent of all tuberculous persons have had lesions which responded to the natural defense mechanisms of the body without the aid of special therapy In some instances in which cure has been ascribed to a particular type of treatment, recovery has really *been brought about by this natural defense* mechanism Patients with old calcified primary tuberculous complexes those with apical, nodular fibrotic areas and those with adhesions and scarring caused by old pleurisies are not candidates for hospitalization These patients should be warned however that careful periodic radiologic examinations are necessary for assurance that the arrest of the process has continued since reactivation may occur whenever resistance is lowered On the other hand treatment is mandatory for every patient with symptoms of pulmonary tuberculosis or roentgenologic evidence of unstable disease The importance of treatment in the subclinical stage cannot be overemphasized, for, if delayed until symptoms are well defined, the patient may lose his chance of recovery

Treatment may consist of bed rest alone or in combination with collapse therapy antimicrobial therapy, or surgical excision Prolonged bed rest is an absolute requirement All other treatments are to be considered adjunct therapy Whether bed rest shall be complete or modified depends upon the type of the infection its severity, and the emotional response and cooperativeness of the patient Usually, the initial treatment is complete bed rest, modified as the symptoms of the patient recede The objective of treatment is not only to secure arrest of active progressive lesions but also to prevent complications, such as hemoptysis dissemination of a caseous lesion, and cavity formation

*Bed Rest* —Bed rest when complete requires rest in bed for the entire 24 hours without bathroom or dining room privileges Before the cure is instituted the patient should arrange his personal and family affairs so that complete relaxation of body and mind can be assured The duration of the treatment is largely dependent upon the patient s cooperation For this reason confidence in his physician and belief in his ultimate recovery must be established at once

Whether the patient shall enter a sanatorium or be allowed to remain at home is often a difficult problem to decide Strict isolation is necessary for a patient whose sputum is positive for tubercle bacilli, and *this is difficult except in a sanatorium* Those with noncommunicable disease may remain at home if complete cooperation of patient and family can be obtained Consciously or unconsciously a patient at home will ignore some of the rules designed for his cure In a sanatorium he eats sleeps rests on schedule He observes others suffering from the same disease and the strict discipline becomes less onerous as he watches other patients who adjust themselves to the routine and reap its benefits He notes too the continued ill health of those who fail to cooperate

Bed rest is based upon physiologic principles During rest in bed the motion of the lungs is decreased approximately 75 per cent the lung volume is reduced by 20 per cent and the accompanying decrease in body metabolism reduces the

amount of blood flowing through the parenchyma so that the absorption of toxic products is lessened with alleviation of symptoms This decrease in blood supply reduces the oxygen supply to the lung so that carbon dioxide accumulates in the tissues Since the tubercle bacilli depend upon a constant supply of oxygen for their growth their increase is limited in the presence of the augmented carbon dioxide In addition in the supine position the power of the cilia to expel bacteria and exudates from the bronchi is increased The healing process of fibrosis is enhanced by decrease in the tension of the affected areas This is brought about by reduction of lung volume by lymph stasis and by tissue ischemia and results in increased local tissue defense and repair

The predilection of tuberculosis for the upper lobes of the lungs is another reason for prescribing bed rest According to a theory of Dock's the flow of arterial blood is greatly restricted at the apices of the lungs of most persons when they are in the upright position since the pressure of the column of blood from the right ventricle to the apices of the lungs is equal to or greater than the mean arterial pressure in the pulmonary arteries In the upright position tissue fluid or lymph is not produced by infiltration in the apical area since a pressure of nearly 15 mm Hg is required to overcome the difference in osmotic pressure between the plasma and the pulmonary tissue fluid As a result of the decreased blood flow to the apices of the lungs the increase of carbon dioxide to the alveoli in this area and the removal of oxygen from them will be at a minimum Tubercle bacilli reaching the apical tissues therefore will be in an optimal atomsphere for support of their metabolism As long as the patient remains upright the pulmonary arteries can bring few antibodies to the apical areas and the removal of bacterial products by the lymph or their dilution in the blood is almost inhibited Hence the removal of bacteria by the lymph during the patient's waking hours and the replacement of bacteria with antibodies from the blood are both practically suspended These facts offer some explanation of why tuberculosis gains a foothold in active lively young persons and in adults whose hours of sleep and rest are minimal During the long hours of activity the bacilli enjoy optimal growth conditions For these reasons the ideal treatment of early apical lesions is complete recumbency for most of the 24 hours Assuming any other position for any but minimum periods interferes with the postural management of tuberculous lesions

*Effective Use of Bed Rest*—To give the lung the maximum amount of rest the patient lies on the affected side in order to reduce the pulmonary movements To facilitate necessary drainage the patient may be kept in the Trendelenburg position throughout the day or for 3 hours in the morning and from 3 to 4 hours in the afternoon This position relieves the diaphragm from the downward pull of the abdominal organs decreases the size of the thoracic cavity and reduces the suction effect of the intrapleural negative pressure The mobility of the upper third of the lung is thereby increased and good drainage induced through the bronchi of the diseased area If the Trendelenburg position is not used the patient lies on the affected side most of the time turning on the unaffected side for 10 minutes every third or fourth hour to facilitate drainage Changing of posture it should be noted particularly if the disease is acutely active should be accomplished with the least possible disturbance of the lungs and the least possible expenditure of energy To decrease the movements of the lung further weights are sometimes placed on the chest directly over the lesion of the upper lobe At first half pound bags of shot are used heavier and heavier bags are then gradually substituted for these till the maximum weight the patient can comfortably support is reached

Some physicians prescribe a modified bed rest which allows reclining in bed or on a chaise lounge for approximately 20 hours The patient eats his meals in an adjoining room and has full bathroom privileges No rule can be laid down for the type of bed rest required in cases of tuberculosis it must be adjusted to individual requirements Some patients with advanced tuberculosis may be required to lie horizontally relaxed mentally and physically for 24 hours a day 7 days a week every week for years or until the disease is brought under control

Relaxation is the business of the day each hour of the day is so planned as to give the diseased lung the greatest possible amount of rest with the fewest possible interruptions The amount of activity allowed should be mapped out by the physician Unexciting radio programs light reading and light games may help the patient pass the hours without exertion Some authorities believe that a patient who is to remain at home should first spend several months in a sanatorium to acclimate himself to the strict routine necessary for recovery

The emotional reactions of the patient must be taken into consideration in planning his course of treatment. To obtain his cooperation after the first shock of the diagnosis and overcome his hopelessness and antagonistic attitude requires patience and skill. The patient must be persuaded that if he receives the right care and is cooperative, he can live long and usefully.

Except for the antibiotics, drugs are not usually required in the treatment of tuberculosis, though they may be indicated for the treatment of complications. Sedatives should not be administered for emotional upsets, since they disturb the cough reflex and cause a retention of secretions.

*Symptomatic Treatment of Tuberculosis.—Cough.*—Cough in pulmonary tuberculosis is a purposeful physiologic reflex response to irritation or pressure within the respiratory tract and a mechanical aid to the evacuation of exudative substances within the bronchial tree. For this reason productive cough is a useful process and should not be unduly suppressed. The value of a productive cough in conjunction with postural drainage should therefore be made plain to the patient. Coughing may become habitual because of nervousness, or the patient may be overanxious to produce sputum and overexert himself.

A cough routine can be developed for thorough evacuation of the sputum in the morning or after meals with little or no coughing the rest of the day. An unproductive cough should be suppressed since it only causes irritation and exhaustion. A wracking cough may be controlled by hot drinks in the morning or by a dose of from 15 to 20 drops of aromatic spirits of ammonia before breakfast and complete rest for half an hour before and after that meal. Codeine sulfate $\frac{1}{4}$ gr every 4 hours or dilaudid hydrochloride $\frac{1}{32}$ gr every 4 hours may also give relief as may demerol in 50 milligram doses given orally after meals and at bedtime. The danger of addiction should be borne in mind.

Snug chest binders adjustable in front may prove helpful. If there is a large cavity and the secretion is excessive, instruction in assuming a proper position in bed for drainage of the bronchial tree a number of times a day will relieve the patient of cough during the intervening periods. If the clearing out of the exudation is unsatisfactory, elevation of the foot of the bed 8 or 9 inches may bring adequate evacuation. If the sputum is too tenacious to be raised without undue effort, sipping hot milk, water or lemonade may afford relief. The use of a humidifier or the inhalation of steam is also helpful. When bronchial spasm is present, antispasmodic mixtures may be used. Expectorant drugs may be given to raise the sputum if all other measures fail. Banyai has found that inhalation of a mixture of 10 per cent carbon dioxide and 90 per cent oxygen changes an unproductive cough into a useful one, decreasing the thickness and tenacity of the sputum and reducing the need for other expectorants. Its use is contraindicated after pulmonary hemorrhage or when severe emphysema, acute fibrinous pleurisy, pleurisy with effusion or hypertension is present.

If the cough is aggravated by a secondary infection such as bronchitis, bronchiectasis, or lung abscess, aerosol penicillin may prove helpful. Where cough has been found referable to tuberculous lesions of the larynx or trachea, streptomycin has been used with striking effect.

*Pain.*—Pain is rarely an important symptom, but a pleuritic pain may become distressing and retard recovery. The use of counterirritants like mustard plasters or painting the skin over the affected area with iodine or applications of menthol or oil of wintergreen ointments may be helpful. Strapping with adhesive tape recommended by some may make the patient uncomfortable and dyspneic. Well-fitting chest binders are more effective. Pain in the lower back may be the result of being propped up in bed or of muscular strain from a sagging bed. A board beneath the mattress or a firm mattress may lessen the discomfort. Aspirin, empirin or codeine may be given if required. An injection of 10 cc. of a 1 per cent procaine solution with 1:25,000 epinephrine hydrochloride into the skin, thoracic wall or parietal pleura has been recommended.

Laryngeal pain is a common complication of pulmonary tuberculosis, the laryngeal

tuberculosis is caused by infective sputum or by bacilli carried to the larynx by the blood stream. The cooperation of the patient must be secured in this case by explaining the need for complete silence to give the larynx a rest. The patient may communicate by writing or, when absolutely necessary, by whispering. Cocaine pastilles may be sucked to relieve the pain or a solution 1 to 5 per cent cocaine used as a spray, but the latter entails some danger. Sulfonamide powder (5 to 10 gr.) blown into the larynx twice a day has proved effective in some cases. Beckman recommends orthoform emulsion self-administered through a Yankauer laryngeal medicator or iodoform weighted with a small amount of talcum. The latter is for insufflation but is preceded by a spray to prevent coughing. In some instances the discomforting pain has been dispelled by gargling with bicarbonate of soda in water on awakening in the morning.

*Hemoptysis.*—The fright of the patient following hemoptysis must be allayed by assurance that it is not a dangerous symptom. Slight streaking of sputum does not require treatment, but moderate bleeding demands absolute rest with partial propping up in bed so that the blood can flow out of the mouth. All movements should be restricted. Coughing up of clots may prevent obstruction of the bronchi; on the other hand, severe coughing may lead to aspiration of contaminated blood into healthy alveoli. Anemia resulting from loss of blood can be treated by administration of ferrous sulfate or gluconate, 12 to 15 gr., with meals. Blood transfusion may be advisable. Restriction of the diet to cold food and drinks for a while has been suggested. If the prothrombin content of the blood is low, vitamin K may be helpful. Enemas or cathartics to prevent straining at stool are advised. Narcotics, particularly morphine, should not be used to the point of inhibiting the cough reflex. In persistent or repeated severe hemorrhage, artificial pneumothorax or pneumoperitoneum may be indicated in order to relax the lung. This should be delayed for a few days, however, until the air passages are free from accumulated blood; this will diminish the chance of the development of the acute pneumonic reactions and serofibrinous pleurisy that may follow pneumothorax. If pneumothorax and pneumoperitoneum fail, other forms of collapse therapy should be considered, such as extrapleural pneumothorax or diaphragmatic paralysis.

*Fever and night sweats* resulting from inadequate rest, poorly ventilated rooms or too much clothing seldom occur after the patient is under hospital routine. Absolute bed rest, fresh air and mental relaxation usually produce remission of these symptoms. Fever wasting the strength of the patient may be relieved or prevented by administration of aspirin or phenacetin, 5 to 10 gr. (0.32 to 0.65 Gm.), acetanilid, 3 gr. (0.2 Gm.), or aminopyrine, 5 gr. (0.32 Gm.). Atropin sulfate, 1/200 to 1/100 gr. (0.32 to 0.65 mg.), or agaricin, ½ gr. (30 mg.), taken not more than three times in 24 hours may be used for persistent night sweats, but the results are frequently disappointing. Some prefer camphoric acid, 20 to 30 gr. (1.3 to 2 Gm.), an hour or two before the sweating usually occurs. An alcohol rub or a bath with tepid water containing 15 gr. (1 Gm.) of alum may prevent attacks of sweating.

*Digestive upsets* and *anorexia*, particularly before proper adjustment to the regimen is made, are not uncommon symptoms in tuberculous patients. Complete rest just before and after meals with stimulation of the appetite by protamine zinc insulin, tinctures of nux vomica, gentian or cardamon has been suggested as helpful treatment. Sodium bicarbonate, 15 gr. (1 Gm.), or 2 cc. of aromatic spirits of ammonia dissolved in warm water may relieve postprandial distress; if these bring no relief, dilute hydrochloric acid may be of value. Nausea may be relieved by application of an icebag to the abdomen. Use of a stomach tube will relieve vomiting. Calcium salts taken orally, calcium gluconate given intramuscularly, or either of these administered intravenously may be used to relieve diarrhea unless this is due to extensive intestinal ulceration. It may be due to dietary factors. Investigation must be made as to the cause of any serious diarrhea, since it may result from general toxemia

hypochlorhydria, or intestinal tuberculosis Amyloid disease may cause the diarrhea in cases of long-standing cavitation and mixed infection

Enteritis is generally the result of a general lowering of resistance and is difficult to control when once established Milk in excess should be avoided and meals should be small in bulk Calcium gluconate (10 cc of a 5 per cent solution) given intravenously has been recommended, as have oral doses of calcium Pain in enteritis may be relieved by tight bandaging of the abdomen

Constipation may be relieved by proper diet and training in regular bowel habits Mild laxatives are sometimes indicated or from ½ oz to 1 oz of mineral oil at bedtime One or two glasses of water half an hour before meals may be helpful

A well balanced diet of from 2500 to 3500 calories will usually prove adequate for tuberculous patients It has been well said that malnutrition is a result rather than a cause of tuberculosis and is not an evidence of metabolic disturbance For this reason, restoration of normal weight in the tuberculous patient is best accomplished by properly treating the tuberculosis Overfeeding is unnecessary, and overweight may tax the pulmonary function The patient should have three meals a day without between meal feeding unless he is unable to take sufficient food at meal time The forcing of milk on a patient is not recommended it may upset the digestion in some and may be distasteful to others Milk nevertheless is a most desirable food and several glassfuls should be included in the daily diet

The food given the tuberculous patient should be attractive and palatable The vitamin intake particularly the intake of vitamins A and C deficiency in which causes pathologic changes in the mucous membranes that may lead to bronchial occlusion should be carefully regulated A complication like bronchial occlusion may be prevented by giving the patient cod liver oil (⅓ oz daily) supplemented with orange or tomato juice (2 to 4 oz after meals) The cod liver oil should be made as palatable as possible Vitamin C may be administered as synthetic ascorbic acid

*Insomnia* —Unadjusted nervous tuberculous patients may suffer from insomnia A tactful discussion of the cause of their nervousness and the need for its control, with assurance that sleeplessness is the result of habit, may relieve the insomnia Visitors in the evening, or visitors who stay too long or talk of disturbing things may be a cause of the upset A comfortable bed is a necessity Proper ventilation of the room, gentle sponging and massage and a hot drink at bedtime may bring a degree of comfort Sedatives, if required, should be discontinued as soon as possible

*Psychotherapy* —Psychologic management of the tuberculous patient is an important part of treatment for the cooperation of the patient in following the prescribed regimen and his belief in the efforts of the physician and in the hope of cure are necessary for recovery The patient should be told the nature of his disease and the possible length of his illness The need for long continued and absolute rest in bed should be explained to him He must be made to understand that there is no short cut to recovery that recovery depends on following without question a regimen that has cured others And, since mental and emotional as well as physical relaxation is imperative, the patient s psychologic maladjustments should be corrected

A patient with minimal disease may require no more treatment than bed rest His progress will be determined by clinical laboratory and radiologic studies Changes in temperature, pulse rate and sedimentation rate, weight maintenance and the appearance or nonappearance of tubercle bacilli in the sputum or gastric contents will indicate the results of bed rest Early abatement of symptoms may indicate improvement but until the sputum becomes negative and *x* ray findings indicate a healing process strict bed rest must continue Asymptomatic patients with active minimal lesions require from 6 to 12 months of continuous rest if the lesions are extensive the patients require from 18 months to 2 or more years of such rest It has been noted that improvement as a result of bed rest is greatest in the first month and that the improvement gradually decreases with time

When sufficient clinical improvement is evident the patient may be allowed to sit up for 15 or 30 minutes daily the amount of time being increased every 2 or 3 weeks The first modification of complete bed rest usually consists in allowing one or two trips to the bathroom wheelchair trips to the treatment room and minor occupational therapy in bed for not more than one hour daily Occupational therapy is allowed for 2 hours when the patient has received full bathroom privileges and he is occasionally allowed to attend church services and movies and engage in other recreations afforded in the sanatorium The patient is fully dressed on these occasions The patient walks to the treatment rooms and to the bathroom and takes his own bath Another privilege is reading studying and listening to the radio during the morning rest hours The patient next becomes ambulatory is fully dressed makes his own bed keeps his room clean and begins supervised activities for 1 to 2 hours daily These hours of activity are gradually lengthened All through these periods of increasing activity up to the time of discharge the patient obeys the rules of absolute bed rest between 1 00 P M and 3 00 P M and lights-out at 9 00 P M The length of time between each period of increased freedom varies with each patient and is entirely dependent upon evident progress in recovery

Often bed rest is sufficient for cure Mitchell reported that of 289 patients with uncomplicated minimal pulmonary tuberculosis followed for 7 or more years after discharge only 37 per cent had one or more reactivations Except for 3 per cent who died and 4 per cent who remained chronically ill all were well and working

Patients who do not respond satisfactorily to complete bed rest require additional therapy such as antimicrobial therapy collapse therapy or surgical intervention or a combination of these

*Antimicrobial Therapy* —The antibiotics although neither a substitute for bed rest nor a substitute for collapse therapy or surgical treatment have opened a new era in the treatment of pulmonary tuberculosis Removal of even a segment of a lung was a dangerous procedure before the advent of the antibiotics but as now used preoperatively and postoperatively these agents have made lung surgery a common method of therapy (See page 985)

*Mechanical and Surgical Therapy of Tuberculosis* —The purpose of collapse therapy is to promote healing of the tuberculous process through relaxation of the lung The volume of the lung is thereby decreased and its physiologic activity lessened as is shown by reduction in ventilation vital capacity and oxygen uptake together with decreased flow of blood and lymph Despite prolonged bed rest a cavity may refuse to heal but when the elastic pull on the cavity walls is relieved by collapse of the lung these walls come together and healing is made possible The parts under the greatest elastic tension recoil the most this brings about shrinkage of the cavity and scar retraction complete closure may follow Meanwhile decreased lymph flow diminishes transport of toxic material from the diseased areas into the general circulation and lessens the toxic symptoms The attendant relative tissue anoxia and lymphostasis apparently enhance fibrosis and diminished oxygenation of the tissues produces conditions unfavorable to growth of the tubercle bacilli

*Artificial pneumothorax* like pneumoperitoneum and phrenic paralysis are reversible processes wheras thoracoplasty is irreversible Each has its place The popularity of artificial pneumothorax has somewhat waned since the possibilities of the other methods have become defined

Indications for the use of pneumothorax are (1) a progressive tuberculous process (2) continued positive sputum (3) cavitation and (4) uncontrollable hemorrhage A tuberculous spontaneous pneumothorax may be converted into a controlled pneumothorax The success of artificial pneumothorax depends to a large degree upon careful case selection In some cases relaxation of the lung sets up a check valve mechanism in the draining bronchus by narrowing the lumen so that the cavities do not close and may even become enlarged Cavities with thick fibrous walls do not respond to this procedure The best results are achieved in small cavities with infiltrations

that are predominantly nodular or bronchopneumonic. Cavities in the upper lobes without extensive exudation or caseation give excellent response. Extensive pleural fibrosis or adhesions will prevent successful pneumothorax. In the latter case intrapleural pneumonolysis should be undertaken to divide the adhesions between the pleural layers. Otherwise artificial pneumothorax must be abandoned.

An active tuberculous process in the opposite lung is not a contraindication to pneumothorax. A minor lesion in the opposite lung may heal spontaneously. Bilateral pneumothorax is often successful but care must be taken to prevent respiratory embarrassment. Refills may occasionally be given at the same time in well-established and well tolerated bilateral cases.

Artificial pneumothorax is contraindicated in the presence of very large cavities located at the periphery of the lung, cavities with rigid walls, tension cavities, bronchial tuberculosis with severe ulcero granulomatous involvement or fibrostenosis of the bronchial lumen, bilateral miliary tuberculosis, predominantly fibrous tuberculosis of long duration with contraction of the corresponding hemothorax, extensive bilateral tuberculous disease and pronounced pleural thickening. Other contraindications are empyema, bronchial asthma, decompensated heart disease, amyloidosis, and hopeless prognosis. Pregnancy is not a contraindication.

When an early infiltrate spills tubercle bacilli into the surrounding pulmonary tissue, a cavity is formed with an encircling bronchopneumonia. While this acute tissue reaction about the tuberculous focus remains active, interference is contraindicated. Absolute bed rest and streptomycin therapy constitute the only recommended treatment. Collapse therapy at this time may prove harmful since artificial pneumothorax is almost always followed by an acute pleurisy and the collapsed areas begin to organize and fibrose. Bed rest and streptomycin will tend to clear out the exudate and decrease the size of the cavity. After the maximum benefit from these measures has been obtained, collapse therapy may be considered. The smaller the cavity is, the more likely is pneumothorax to be successful. If collapse therapy should fail to control the tuberculous process, major surgery must be attempted.

Refills should be continued for from 2 to 6 years or until the cavities are completely closed. If the sputum remains positive after 6 months, this treatment should be discontinued and other collapse therapy substituted.

The most frequent complication is pleural effusion, occurring in approximately 80 per cent of cases. This may absorb spontaneously or may require aspiration. Since the advent of antimicrobial therapy, the previous incidence of empyema in pneumothorax patients (10 per cent) has been substantially reduced by combined streptomycin and PAS administration before the introduction of pneumothorax. Frequent aspiration and thoracoplasty may be required when it occurs. Other complications occasionally observed are air embolism, pleural shock, surgical emphysema, accidental pneumothorax and hemoptysis.

Failure of the lung to re-expand after pneumothorax is discontinued may require decortication of the fibrinous coverings which have accumulated. When peeled off the lung may readily expand.

*Closed Intrapleural Pneumonolysis.*—In many cases of pulmonary tuberculosis adhesions exist between the visceral and parietal layers of the pleura. These may prevent adequate collapse or relaxation of the lung by artificial pneumothorax. In such cases the adhesions should be severed (intrapleural pneumonolysis), after which the lung will usually collapse satisfactorily.

*Phrenic-nerve crush* is the simplest and safest method of collapse therapy and, although considered the least effective procedure, has frequently produced dramatic results. Many tuberculous patients are unfitted for surgical measures and others fail to have adequate collapse following artificial pneumothorax because of pleuritic adhesions. Rather than submit these patients to continued ineffectual pneumothorax or to prolonged bed rest, it may be preferable to attempt collapse by phrenic nerve block.

Permanent paralysis of the diaphragm

was favored in former years today temporary paralysis is preferred The operation may be repeated once or twice a year if necessary, if closure of the cavity and arrest of the disease has been achieved or it may be made permanent in selected cases. Paralysis of the diaphragm may be supplemented by pneumoperitoneum to increase the elevation of the diaphragm and effectiveness of the operation

*Pneumoperitoneum* —Pneumoperitoneum is a simple and safe method of collapsing the lung without causing the complications that follow artificial pneumothorax It may be used in cases considered unsuitable for pneumothorax or thoracoplasty Artificial pneumothorax produces collapse of the lung by direct action of the air in the thorax Pneumoperitoneum on the contrary produces relaxation of the lung by increasing the air pressure under the diaphragm thus causing it to rise high in the chest

When combined with streptomycin therapy pneumoperitoneum has proved a method of choice for patients with bilateral tuberculous disease with fibrotic changes cavitation and marked or moderate exudation In exudative bilateral tuberculous disease that precludes use of pneumothorax and major surgery this combined treatment is often of great value

*Intracavitary suction drainage* as suggested by Monaldi is drainage of a cavity by introduction of a catheter into it through the chest wall It is indicated for patients with large ballooned cavities connected with stenosed bronchi This procedure succeeds in diminishing and sometimes closing cavities

This procedure is advocated in cases in which previous collapse therapy or low vital capacity forbids continued collapse treatment or resection

*Oleothorax* is a procedure now rarely used It consists of instilling a vegetable oil treated with Gomenol or other mild antiseptic into an intrapleural pneumothorax space

*Other Forms of Mechanical Therapy* —Various types of mechanical therapy advocated in the past are rarely used today Such procedures include scalenotomy scalenectomy (division or partial resection of the scalene muscles) open cavity drainage and multiple intercostal nerve paralysis Other methods have been found more effective

Such nonsurgical mechanical aids to immobilization and compression therapy as sand or shot bags hammocks or swings corsets and braces continue to be used Very good results have been reported from the use of the Barach equalizing pressure chamber but because the equipment is expensive it is not generally available The results obtained have been sufficiently favorable to indicate that this method of treating pulmonary tuberculosis is worthy of further study

*Other Forms of Surgical Therapy* —Other surgical procedures for pulmonary tuberculosis than those discussed include thoracoplasty lobectomy pneumonectomy and segmental pulmonary resection Resections are being attended with encouraging results due largely to the use of streptomycin

A thorough knowledge of the physiologic function of the patient s lung and its pathologic affections must be obtained before mapping out a therapeutic program The physician s task does not stop with arrest of the disease it continues with planning the patient s rehabilitation and maintaining constant vigilance against reactivation of his tuberculous process Beyond this lies the equally great task of preventing the spread of tuberculosis This involves early diagnosis and treatment of cases and immunization of the public against the disease in so far as such immunization can be achieved

*Note on BCG Vaccination* —The subject of immunity to tuberculosis though it has been the subject of intensive investigation is still a controversial issue For a critical review of the matter the reader is referred to Rich A *The Pathogenesis of Tuberculosis* Charles C Thomas 1944 and to Lurie Max B Natural and Acquired Resistance to Tuberculosis *Am Jr of Medicine* Vol IX (Nov ) 1950

Many vaccines have been prepared and used from time to time to increase resistance to tuberculosis None have withstood the test of time Vaccination with the Calmette Guerin bacillus holds the greatest interest today Calmette and Guerin cultivated a highly virulent bovine tubercle bacillus (isolated by Nocard from the udder of a tuberculous cow in 1902) on a medium con

sisting of potato cooked in 5 per-cent glycerinated ox bile. After 236 transplantations on this medium, the virulence of the organism was lost for laboratory animals and cattle. Despite the organism's loss of virulence, however, vaccination with this attenuated culture gave cattle considerable protection against virulent infection with bovine tubercle bacilli.

In 1922, Weill Hall was the first to give the vaccine orally to newborn babies of tuberculous mothers. No untoward effects followed its administration. Indeed, in such infants less clinical tuberculosis developed than in unvaccinated infants of tuberculous mothers. BCG mass vaccination first by the oral route and subsequently by the intracutaneous route was soon afterwards used widely in France, the Scandinavian countries, Spain, Russia, and the Balkan States. In the United States vaccination of infants and children with BCG was begun in 1926 in New York City by Park and his associates. This work is still in progress.

One of the most painstaking BCG-vaccination studies in this country has been carried out among American Indians by Aronson and his associates. A report of the outcome of his well controlled work from nine to eleven years after the vaccinations shows that of 1551 BCG-vaccinated Indians only six died of tuberculosis, whereas of 1457 Indians not vaccinated with BCG 38 died of the disease.

It is therefore apparent that though BCG vaccination may not confer complete immunity to tuberculosis, it nevertheless does reduce the mortality rate for tuberculosis among persons exposed to the disease.

Among the many hundreds of thousands of persons to whom the vaccine has been given, there is no evidence of a single death that can be attributed directly to the vaccine. The disaster in Lubeck, Germany (where many infants who supposedly received BCG fell ill—some died of tuberculosis) was apparently due to contamination of the vaccine with virulent tubercle bacilli.

It should be stated that, in the United States and Great Britain, where antituberculosis progress has been outstanding, BCG vaccination is not received with any enthusiasm. Indeed, some authorities in this country (like J. Arthur Myers) are strongly opposed to mass vaccination with BCG.

"The tuberculin reaction," he says, "indicates the presence of sensitivity to tuberculoprotein and has not been demonstrated to be a criterion of immunity. The temporary fixing power of allergic tissue was formerly misinterpreted as indicating immunity. No test has been devised to identify or measure immunity."

*Indications for Use of BCG.*—BCG vaccination is recommended for tuberculin-negative persons, such as nurses, attendants, interns, and others exposed to tuberculous patients or to material containing viable and virulent tubercle bacilli. It is also indicated for use in badly contaminated regions, regions in which social and economic conditions favor the spread of tuberculosis, to protect infants and young adults from infection.

*Contraindications.*—BCG vaccination is not recommended for (1) persons who have a tuberculin-positive reaction, (2) persons suffering from any infectious skin condition (such as impetigo), (3) persons recently vaccinated with smallpox vaccine, (4) persons suffering from pyrexia, malaise, or other subjective symptoms, or (5) premature or underweight infants.

In progressive countries, countries in which efficient health measures have reduced the mortality rate for tuberculosis to a low level, the advantages to be gained from BCG are not likely to be great.—Editor.

## REHABILITATION

Rehabilitation of the tuberculous patient was defined at the Washington Conference on Rehabilitation of the Tuberculous as "any services necessary to render a tuberculous patient fit to engage in a remunerative occupation suitable to health and aptitude." Recovery of the tuberculous patient, therefore, means more than arrest of this disease; it means restoration to a normal life. As Murray has said, "Morally and economically the doctor who takes care of a patient's illness can no longer wash his hands of the problem when the medical condition is cured. His problem must include the restor

ation of the patient to usefulness Establishment of hope and belief in ability to recover must be instilled early in the patient and maintained all through the *long period of treatment*

The seasoning of the convalescent patient to limited hours of work that increase with gain of strength often begins with light suitable work around the sanatorium If *reasonable amounts of work are alloted* this activity promotes a purposeful exercise and helps the patient to begin the readjustment to everyday life

Approximately 50 per cent of the recovered *patients are said to return to their* former jobs either part or full time Others may have done work that would now be too demanding upon their strength and for these vocational guidance may be required *Psychotherapist physiotherapist* social worker and social agencies work together to fit the patient into a new job and find the particular niche he is best fitted to fill The former training of the patient should always be *taken into consideration*

## PROGNOSIS IN TUBERCULOSIS

Prognosis in pulmonary tuberculosis must always be *guarded cure can never* be certain Those with apparent arrest of the disease are subject to reactivation at any time Patients with minimal disease after prolonged bed rest and antimicrobial and collapse therapy *may nevertheless gradually* succumb to the disease The risk of these patients dying within a few years is always greater than that of the rest of the general population This risk is increased manyfold in those with *moderately* advanced tuberculosis whatever treatment is administered For those with far advanced disease the prognosis is always grave

The prognosis depends upon consideration of a number of factors The extent of the lesion at the time therapy is initiated is important According to studies reported life expectancy for patients with early or limited lesions without cavity formation is much better than it is for patients with moderately advanced disease It has been estimated that a third of the latter did not survive after five years until the advent of the antibiotics Those with far advanced disease do not usually survive for more than from 2 to 5 years without special therapy Today with antimicrobial therapy collapse *therapy and radical pulmonary surgery a* surprising number of these seemingly hopeless patients survive

The nature of the lesion also has a bearing on the outcome of treatment Lesions of *the fibroid nodular type tend to respond* well to treatment whereas those of the exudative bronchopneumonic type although they sometimes resolve tend to maintain unresolved caseous cores These are apt to *be sloughed off into the bronchial tree and* disseminate into the surrounding parenchyma Again the size of the cavity has an affect upon the prognosis Cavities over 2 cm in diameter are difficult to obliterate by *collapse therapy* and *unless* arrest of the process can be secured by resection death usually occurs within five years On the other hand a small fibrous cavity may cause a continuously positive sputum *but the patient has a good life expectancy* Cases in which there are very large cavities can rarely be controlled and care of such cases in sanatoria is for relief of the victims symptoms and for the protection of the *public*

The clinical symptoms as Amberson points out likewise serve as a partial index to the prognosis An older person without fever has a better chance of recovery than a *young one with prolonged fever* A patient with a small amount of sputum may have no extension for years whereas a large amount of liquid sputum may indicate early extension Prognosis is better when the tubercle bacilli are scarce this indicating that the cavity walls are not undergoing active necrosis A patient with normal temperature pulse and sedimentation rate has a good outlook Age and race are additional factors affecting prognosis Tuberculosis in the young is more serious than in older persons Recovery from tuberculosis is less frequent in the negro than in the white race

Prognosis is most favorable when diagnosis is made early and treatment is prompt and adequate Once a patient s disease is apparently arrested and he is discharged

sisting of potato cooked in 5 per cent glycerinated ox bile After 230 transplantations on this medium the virulence of the organism was lost for laboratory animals and cattle Despite the organism's loss of virulence however, vaccination with this attenuated culture gave cattle considerable protection against virulent *infection* with bovine tubercle bacilli

In 1922 Weill-Hall was *the first to give* the vaccine orally to newborn babies of tuberculous mothers No untoward effects followed its administration Indeed in such infants, less clinical tuberculosis developed than in unvaccinated infants of tuberculous mothers BCG *mass vaccination first* by the oral route and subsequently by the intracutaneous route was soon afterwards used widely in France the Scandinavian countries, Spain Russia and the Balkan States In the United States, vaccination of infants and children with BCG was begun in 1926 in New York City by Park and his associates This work is still in progress

One of the most painstaking BCG—vaccination studies in this country has been carried out among American Indians by Aronson and his associates A report of the outcome of his well-controlled work from nine to eleven years after the vaccinations shows that of 1551 BCG—vaccinated Indians only six died of tuberculosis whereas of 1457 Indians not vaccinated with BCG *53 died of the disease*

It is therefore apparent that though BCG vaccination may not confer complete immunity to tuberculosis it nevertheless does reduce the mortality rate for tuberculosis among persons exposed to the disease

Among the many *hundreds of thousands* of persons to whom the vaccine has been given, there is no evidence of a single death that can be attributed directly to the vaccine The disaster in Lubeck Germany (where many infants who supposedly received *BCG fell ill—some died of tuberculosis*) was apparently due to contamination of the vaccine with virulent tubercle bacilli

It should be stated that, in the United States and Great Britain, where antituberculosis progress has been outstanding BCG vaccination is not *received* with any enthusiasm Indeed some authorities in this country (like J Arthur Myers) are strongly opposed to mass vaccination with BCG

'The tuberculin reaction he says, 'indicates the presence of sensitivity to tuberculo protein and has not been demonstrated to be a criterion of immunity The *temporary fixing power of allergic tissue* was formerly misinterpreted as indicating *immunity No test has been devised to* identify or measure immunity

*Indications for Use of BCG* —BCG vaccination is recommended for tuberculin negative persons, such as nurses attendants, interns, and others exposed to tuberculous patients or to *material containing viable* and virulent tubercle bacilli It is also indicated for use in badly contaminated regions, regions in which social and economic conditions favor the spread of tuberculosis to protect infants and young adults from infection

*Contraindications* —BCG vaccination is not recommended for (1) persons who have a tuberculin positive reaction (2) persons suffering from any infectious skin condition (such as impetigo) (3) persons recently vaccinated with smallpox vaccine (4) persons suffering from pyrexia malaise or other subjective symptoms or (5) premature or underweight infants

In progressive countries countries in which efficient health measures have reduced *the mortality rate for tuberculosis to a low* level the advantages to be gained from BCG are not likely to be great —Editor

## REHABILITATION

*Rehabilitation of the tuberculous patient* was defined at the Washington Conference on Rehabilitation of the Tuberculous as any services necessary to render a tuberculous patient fit to engage in a remunerative occupation suitable to health and aptitude Recovery of the tuberculous patient therefore means more than arrest of this disease it means restoration to a normal life As Murray has said Morally and economically the doctor who takes care of a patient s illness can no longer wash his hands of the problem when the medical condition is cured His problem must include the restor

JENNINGS F I Pregnancy and Tuberculosis In Hayes F W —Ibid
KAYNE, G C PAGEL W and O SHAUGHNESSY I Pulmonary Tuberculosis London Oxford Univ Press 2nd ed 1948
LAMBERT FORJAN Pulmonary Tuberculosis In Conn H F —Ibid
LOWRY T Diseases of the Pleura In Myers J A and McKinlay C A —Ibid
and McKinlay C A Chest and Heart Springfield Charles C Thomas 1948 v 1
MARIETTA S U Tuberculosis and Diabetes In Hayes F W —Ibid
McKELVEY, J I Tuberculosis in Obstetrics In Myers and McKinlay —Ibid v 2
MYERS J A and McKINLAY C A The Chest and Heart Springfield Charles C Thomas 1948
NATIONAL TUBERCULOSIS ASSOCIATION Diagnostic Standards and Classification of Tuberculosis New York 1950
RUBIN J H and RUBIN M Diseases of the Chest Phila Saunders 1947
SALKIN DAVID Pulmonary Tuberculosis In Pillmore G U Clinical Radiology Phila Davis Co 1950
SKOOLAND J I Tuberculosis of Nervous System In Myers and McKinlay Ibid v 2
THOMAS C J Tuberculosis of the Genitourinary System In Hayes F W Ibid

### Miliary Tuberculosis

HEAD J R Miliary Tuberculosis In Kayser F A Therapeutics in Internal Medicine New York Nelson 1950
LEVINE E R Classification of Reinfection Pulmonary Tuberculosis In Hayes W L Fundamentals of Pulmonary Tuberculosis Springfield Charles C Thomas 1949
LINCOLN E M and KIRAUSE T W Chemotherapy of Tuberculosis in Children Pediatrics 1950 5 280-95
MEDICAL RESEARCH COUNCIL Streptomycin in Acute Miliary Tuberculosis Lancet 1950 1 841-46
WALKER A M HINSHAW H C and BARNWELL J B Streptomycin in the Treatment of Tuberculosis in Man In Waksman S A Streptomycin Nature and Practical Applications Baltimore Williams & Wilkins 1949
WHITEHOUSE F R Treatment of Generalized Miliary and Meningeal Tuberculosis with Streptomycin and Promizole Virginia Med Month 1950 77 227 31

### Tuberculosis in Older Patients

AUERBACH OSCAR and GREEN HENRY Pathology of Tuberculosis in the Older Ages Quart Bull Sea View Hosp 1940 5 237 61
LEECH E L Problems Presented by Pulmonary Tuberculosis in Patients over Fifty Ann Int Med 1950 33 321 32
MYERS J A M Tuberculosis Among Persons Over Fifty Years of Age Geriatrics 1946 1 27-35 456

### Treatment of Tuberculosis

ALEXANDER JOHN Collapse Therapy in Pulmonary Tuberculosis Springfield Charles C Thomas 1937
ARMSTRONG B W et al Bed rest Collapse and Streptomycin in Treatment of Pulmonary Tuberculosis Dis Chest 1950 17 503-08
BADGER T L and PATTON W E Recent Advances in the Treatment of Pulmonary Tuberculosis M Clin North America 1950 34 1363-80
BAGGENSTOSS A H FELDMAN W H and HINSHAW H C Effect of Streptomycin on the Pathology of Generalized Miliary and Meningeal Tuberculosis Proc Staff Meet Mayo Clin 1947 22 265-74
BANYAI A L Pneumoperitoneum Treatment St Louis C V Mosby Co 1946
BOGEN EMIL Streptomycin Dosage in Treatment of Tuberculosis Dis Chest 1949 16 761 64
BRAINARD H D and PAGLE H R Effect of Streptomycin in Tuberculous Meningitis Ann Int Med 1950 33 397-410
BRANTIGAN O C and RIGDON H L Extrapleural Pneumolysis with Lucite Ball Plombage Dis Chest 1950 18 277 90
BROCK B L Streptomycin and Artificial Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis Dis Chest 1951 19 411 23
BUNN P A Miliary and Meningeal Tuberculosis Tr 9th Streptomycin Conf Vet Admin 1950 118
CAIRNS H SMITH H V and VOLLUM R L Tuberculous Meningitis J A M A 1950 144 92
CANADA R O et al Three-year Follow up of 202 Cases of Pulmonary Tuberculosis Treated with Streptomycin Tr 9th Streptomycin Conf Vet Admin 1950 69
CHAMBERLAIN J M and KLOPSTOCK R Further Experience with Segmental Resection in Tuberculosis J Thoracic Surg 1950 20 843-53
COUNCIL ON PHARM AND CHEM A M A Current Status of Chemotherapy of Tuberculosis in Man J A M A 1950 142 650-51
CUTLER J W Importance of Extrapleural Pneumothorax in the Collapse Therapy of Pulmonary Tuberculosis J Thoracic Surg 1951 21 217 59
DAY J E et al Resection in the Treatment of Pulmonary Tuberculosis J Thoracic Surg 1950 20 854 65
DUNNER EDWARD and BROWN W B Streptomycin para aminosalicylate in the Treatment of Pulmonary Tuberculosis Dis Chest 1951 19 438-43
EDLIN J S and BASSIN SYDNEY Pneumoperitoneum Versus Pneumothorax New York St J Med 1950 50 1947 55

from the sanatorium after care plays an important role

## REFERENCES

*Introduction*

ANDERSON R J Observations on Mass Survey and Hospital Admission X ray Programs, J Lancet 1950 *70* 145

GURALNICK L and GLASER S Tuberculosis Mortality in the United States Pub Health Report 1950 *65*, 14

*Pathogenesis*

KAYNE G G PAGEL W and O SHAUGHNESSY L Pulmonary Tuberculosis London Oxford Univ Press 1948 2nd ed

LEVINE E R Classification of Pulmonary Tuberculosis In Hayes E W Fundamentals of Pulmonary Tuberculosis and its Complications Springfield Charles C Thomas 1949

MEDLAR E M Pathogenesis of Minimal Pulmonary Tuberculosis Amer Rev Tuberc 1948 *58* 583

NATIONAL TUBERCULOSIS ASSOCIATION Diagnostic Standards and Classification of Tuberculosis 1950 ed

SWEANY H C and BOGEN EMIL Bacteriology Infection and Pathology of Tuberculosis In Hayes E W —*Ibid*

*Classification*

JACKSON C L and HUBER J F Correlated Applied Anatomy of Bronchial Tree and Lungs with System of Nomenclature Dis Chest 1943 *9* 319-26

LEVINE L R Classification of Reinfection Pulmonary Tuberculosis In Hayes E W Fundamentals of Pulmonary Tuberculosis and its Complications Springfield Charles C Thomas 1949

MYERS J A Primary Tuberculosis In Hayes E W —*Ibid*

NATIONAL TUBERCULOSIS ASSOCIATION Diagnostic Standards and Classification of Tuberculosis 1950 Edition

*Clinical Manifestations*

DAVIDSON M Practical Manual of Diseases of the Chest London Oxford Univ Press 3rd ed 1948

KAYNE G C PAGEL W and O SHAUGHNESSY L Pulmonary Tuberculosis London Oxford Univ Press, 2nd ed 1948

PEABODY J W Diagnosis of Reinfection Pulmonary Tuberculosis In Hayes E W Fundamentals of Pulmonary Tuberculosis and its Complications Springfield Charle C Thomas 1949

SALKIN, DAVID Pulmonary Tuberculosis In Pillmore G U Clinical Radiology Phila F A Davis Co 1950

*Diagnosis*

ABBOTT O A Clinical Significance of Pulmonary Hemorrhage Study of 1 316 patients with Chest Disease Dis Chest 1948 *14* 824-42

BANYAI A I Clinical Value of Examination of Gastric Contents for Tubercle Bacilli Am J Med 1948 *4* 836

——Differential Diagnosis of Reinfection Pulmonary Tuberculosis In Hayes, E W Fundamentals of Pulmonary Tuberculosis Springfield Charles C Thomas 1949

GARLAND L H Conditions to be Differentiated in Roentgen Diagnosis of Pulmonary Tuberculosis Ann Int Med 1948 *29* 878-80

HATA D JR VENTERS H D JR and CUMMINGS M M Efficiency of Different Laboratory Examinations in Diagnosis of Pulmonary Tuberculosis Dis Chest 1950 *18* 352 62

KATZ SOL *et al* Diagnostic Importance of Bone Marrow Examination in Acute Hematogenous Tuberculosis M Clin North America 1950 1817 28

KAYNE G C, PAGEL W and O SHAUGHNESSY L Pulmonary Tuberculosis London Oxford Univ Press 2nd ed 1948

NATIONAL TUBERCULOSIS ASSOCIATION Diagnostic Standards and Classification of Tuberculosis New York 1950

PEABODY J W Diagnosis of Reinfection Pulmonary Tuberculosis In Hayes, E W Fundamentals of Pulmonary Tuberculosis Springfield Charles C Thomas 1949

SINGER J J Differential Diagnosis of Chest Diseases Philadelphia Lea & Febiger 1949

*Complications*

BANYAI A I Differential Diagnosis of Reinfection Pulmonary Tuberculosis In Hayes E W —*Ibid*

COHEN S S Tuberculosis of Larynx In Hayes E W Fundamentals of Pulmonary Tuberculosis and Its Complications Springfield Charles C Thomas 1949

——Tuberculosis of the Respiratory Passages and the Auditory System In Myers and McKinlay *Ibid* v 2

COOK E N GREENE L F and HINSHAW H C Streptomycin in Treatment of Tuberculosis of the Urinary Tract Trans Proc Mayo Clin 1946 *21* 277

CULLEN J H Intestinal Tuberculosis a Clinical Pathologic Study Quart Bull Sea View Hosp 1940 *5* 143-60

FELLER E P Pulmonary Tuberculosis In Conn H F Current Therapy Philadelphia Saunders 1950

GEER E K Pulmonary Tuberculosis In Watson C J Outlines of Internal Medicine Dubuque Brown Co 1949

HAYES E W and ADAMES A A Tuberculosis of Abdomen In Myers and McKinlay *Ibid* v 2

Weis M and Finucane D L Bronchiectasis Secondary to Tuberculosis Scientific Exhibit National Tuberculosis Association Meeting Washington D C April 1950
Wilson N J and Overholt R H Major Surgical Procedures in the Treatment of Pulmonary Tuberculosis In Hayes E W Fundamentals of Pulmonary Tuberculosis Springfield Charles C Thomas 1949
Woodruff W and Merkel C G Monaldi Drainage Valuable Adjunct in Surgical Treatment of Pulmonary Tuberculosis New York St J Med 1950 50 201-06
Wright G W Place R and Princi F Physiologic Effect of Pneumoperitoneum Upon the Respiration Am Rev Tuberc 1949 60 706-14

*BCG Vaccination*

Aronson J D Protective Vaccination Against Tuberculosis with Special Reference to BCG Vaccination Am Rev Tuberc 1948 5 255
Calmette A Guerin C and Breton M Contribution a l'etude de la Tuberculose Experimentale du cobaye Ann Inst Pasteur 1907 21 401
Kereszturi C Park W and Schick B Intracutaneous BCG Vaccination Am J Dis Child 1932 43 273
McDougall John B Tuberculosis A Global Study in Social Pathology Edinburgh E & S Livingstone Ltd 1949
Principles and Application of BCG Vaccination Bureau of Tuberculosis Control Dept of Health Commonwealth of Penna

*Rehabilitation*

Heaf Frederick Value of Work in Treatment of Tuberculosis Lancet 1945 1 263 64
Heaf F R G Aftercare and Re-ablement for the Tuberculous Pathways in Aftercare Nat Assoc Prevent Tuberc 1946 2-4
Heise F H Importance of Postsanatorium Care of the Tuberculous Am Rev Tuberc 1946 54 344-48
Hudson Holland and Kiefer N C Rehabilitation of the Tuberculous Proc Conf on Rehabilitation of the Tuberculous Nat Tuberc Assn 1946
Kiefer N C Present Concepts of Rehabilitation in Tuberculosis Review of the Literature 1938-1947 Nat Tuberc Assn 1948
Murray C R Medical Progress Trends and Progress in Rehabilitation of the Sick and Injured New York Med 1946 2 11 21 22 36
Siltzbach L E Clinical Evaluation of Rehabilitation of the Tuberculous Nat Tuberc Assn 1944
Small Benjamin Rehabilitation as a Coordinated Effort Bull Nat Tuberc Assn July 1950 103 104
Tollen W B Why Do Patients Go AWOL? *Ibid* 101 102

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FERSHING, J FREEMAN S *et al* Effect of ACTH on Patients with Pulmonary Tuberculosis J Lab and Clin Med 1950 *36*, 820-21
FISHER M W Streptomycin Resistant Tubercle Bacilli Am Rev Tuberc 1948 *57* 53-57
FOX W A Modified Conception of Phrenic Nerve Crush and Pneumoperitoneum Therapy, Thorax 1950 *5* 191 99
FRIEDMAN L I, DAVENPORT L O and BOHORFOUSH J C Extrapleural *Pneumothorax* Dis Chest 1949 *15* 306-23
GUTHEIL D *et al* Late Results of Thoracoplasty According to Type of Pulmonary Tuberculosis Present Status of 254 Patients Two to Ten Years after Thoracoplasty Am Rev Tuberc 1950 *62* 615-53
*HABEET W J* and REISER H G Pneumoperitoneum with Phrenic Paralysis for Pulmonary Tuberculosis Am Rev Tuberc 1950 *61* 323 34
HAYES E W and ADAMES A A Treatment of Reinfection Pulmonary Tuberculosis In Hayes E W Fundamentals of Pulmonary Tuberculosis and its Complications Springfield Charles C Thomas 1949
HIMMELSTEIN AARON BERRY F B and READ C T Lobectomy and Pneumonectomy in Treatment of Pulmonary Tuberculosis J Thoracic Surg 1950 *20* 866-81
HINSHAW, H C Antimicrobial *Therapy in* Human Tuberculosis Am J Med 1950 *9* 654-61
HOFFMAN S H and HYMAN G A Combined use of Streptomycin and Pneumoperitoneum in Treatment of Pulmonary Tuberculosis Dis Chest 1949 *15* 354
*HUGHES, F J Combined Intermittent Regimens* Employing Streptomycin and Paraminosalicylic Acid in the Treatment of Pulmonary Tuberculosis Tr 9th Streptomycin Conf Vet Admin 1950 36
HURST A and MULLEN T Segmental Collapse in Therapeutic Pneumothorax Radiology 1950 *55* 228-31
JONES J C and ROBINSON J L Pulmonary Resection in Tuberculosis Its Hazards Indications and Results J Thoracic Surg 1950 *20* 882 91
KARLSON A G GAINER J H and FELDMAN W F Effect of Neomycin on Tuberculosis in Guinea Pigs Infected with Streptomycin resistant Tubercle Bacilli Am Rev Tuberc 1950 *62* 345-52
KING D S Medical Progress Tuberculosis New England J M 1950 *243* 530-36
LAIRD R C and LINDERFIELD C F Report of Series of Single-stage Thoracoplasties J Thoracic Surg 1950 *20* 835-42
LINCOLN, E M and KIRMSE T W Streptomycin and Promizole Therapy of Miliary and Meningeal Tuberculosis in Children Am Rev Tuberc 1950 *61* 159-70
LINCOLN N S *et al* Dihydrostreptomycin in *Pulmonary* Tuberculosis Am Rev Tuberc 1950 *62* 572-81
LYGHT C E Toxicity and Stability of Paraminosalicylic Acid (PAS) Tr 9th Streptomycin Conf Vet Admin 1950 p 103
MADIGAN D G *et al* Para aminosalicylic Acid in Tuberculosis Clinical and Pharmalogic Aspects Lancet 1950 *1* 239-45
MATSON R C and CONKLIN W S Simpler Forms of Mechanical Therapy of Pulmonary Tuberculosis In Hayes E I Fundamentals *of Pulmonary Tuberculosis and its Complications* Springfield Charles C Thomas 1949
MITCHELL R S Phrenic Nerve Interruption in the Treatment of Pulmonary Tuberculosis Am Rev Tuberc 1948 *58* 619-45
MOYER R F Pneumoperitoneum and Phrenicclasia in the Treatment of Pulmonary Tuberculosis Dis Chest 1949 *15* 43 59
MYERS J A Tuberculosis Among Children and Adults Springfield Charles C Thomas 3rd ed 1951
NETZER SOLOMON Ten Years of Pneumoperitoneum Am Rev Tuberc 1951 *63* 62 66
OVERHOLT R H WOOD F M and RAMSAY B H Segmental Pulmonary Resection J Thoracic Surg 1950 *19* 207 25
OVERHOLT R H and KENNEY L J One-stage Costoversion Thoracoplasty In Surgical Forum Proceedings of Amer Coll Surgeons 1950 Philadelphia Saunders 1951
PECK W M *and* WILLIS *H S Bed Rest in* Tuberculosis Am Rev Tuberc 1945 *52* 15-20
RYAN T C and LINEBERRY W T A Pneumonectomy for Pulmonary Hemorrhage in Tuberculosis Am Rev Tuberc 1950 *61* 426-30
SCANNELL J G Anatomic Approach to Segmental Resection J Thoracic Surg 1949 *18* 64
SCHWARTZ W S WALTER S T and MOYER R E Aureomycin in Treatment of Tuberculosis Am Rev Tuberc 1950 *61* 875
*SHAMASKIN ARNOLD TB 1 in Pulmonary Tuber*culosis a Study of Toxicity and Bacterial Resistance Tr 9th Streptomycin Conf Vet Admin 1950 p 90
SOKOLOFF MARTIN J Symptomatic Management of Pulmonary Tuberculosi Gen Practitioner 1951 *3* 2
STEENKEN WILLIAM and WOLINSKY E Effects of Antimicrobial Agents on the Tubercle Bacilli and on Experimental Tuberculosis Am J Med 1950 *9* 633-53
SWEET R H Lobectomy and Pneumonectomy in the Treatment of Pulmonary Tuberculosis J Thoracic Surg 1950 *19* 298-303
TEMPEL C W *et al* Combined Intermittent Regimens Employing Streptomycin and Para*minosalicylic Acid in the Treatment of Pulmo*nary Tuberculosis Tr 9th Streptomycin Conf Vet Admin 1950 p 36
VETERAN S ADMINISTRATION STREPTOMYCIN COM Report to the Council on Pharmacology and Chemistry A M A Current Status of Chemotherapy of Tuberculosis in Man J A M A *1950 142* 650-53

WEISS M and FINLAND D L Bronchiectasis Secondary to Tuberculosis Scientific Exhibit National Tuberculosis Association Meeting Washington D C April 1950
WILSON N J and OVERHOLT R H Major Surgical Procedures in the Treatment of Pulmonary Tuberculosis In Hayes E W Fundamentals of Pulmonary Tuberculosis Springfield Charles C Thomas 1949
WOODRUFF W and MERKEL C G Monaldi Drainage Valuable Adjunct in Surgical Treatment of Pulmonary Tuberculosis New York St J Med 1950 50 201-06
WRIGHT C W PLACE R and LUISET F Physiologic Effect of Pneumoperitoneum Upon the Respiration Am Rev Tuberc 1949 60 706-14

*BCG Vaccination*

ARONSON J D Protective Vaccination Against Tuberculosis with Special Reference to BCG Vaccination Am Rev Tuberc 1948 58 255
CALMETTE A CUERIN C and BRETON M Contribution a l'etude de la Tuberculose Experimental du cobaye Ann Inst Pasteur 1907 21 401
KERESZTURI C PARK W and SCHICK B Intradermal BCG Vaccination Am J Dis Child 1932 43 273
McDOUGALL, JOHN B Tuberculosis A Global Study in Social Pathology Edinburgh E & S Livingstone Ltd 1949
Principles and Application of BCG Vaccination Bureau of Tuberculosis Control Dept of Health Commonwealth of Penna

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HEAF F R G Aftercare and Re-ablement for the Tuberculous Pathways in Aftercare Nat Assoc Prevent Tuberc 1946 2-4
HEISE F H Importance of Postsanatorium Care of the Tuberculous Am Rev Tuberc 1946 54 344-48
HUDSON HOLLAND and KIEFER N C Rehabilitation of the Tuberculous Proc Conf on Rehabilitation of the Tuberculous Nat Tuberc Assn 1946
KIEFER N C Present Concepts of Rehabilitation in Tuberculosis Review of the Literature 1938-1947 Nat Tuberc Assn 1948
MURRAY C R Medical Progress Trends and Progress in Rehabilitation of the Sick and Injured New York Med 1946 2 11 21 22 36
SILTZBACH L E Clinical Evaluation of Rehabilitation of the Tuberculous Nat Tuberc Assn 1944
SMALL BENJAMIN Rehabilitation as a Coordinated Effort Bull Nat Tuberc Assn July 1950 103-104
TOLLEY W B Why Do Patients Go AWOL? Ibid 101 102

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*Diagnosis*—The diagnosis may be suspected if there is response to antiluetic therapy Bronchoscopic examination is helpful in indicating the extensiveness of

bronchial involvement and in ruling out other conditions

Response to antiluetic therapy does not necessarily indicate syphilis since improvement may be due to the healing of other pulmonary conditions However, these other pulmonary diseases will recur and will not be affected by a second course of antisyphilitic treatment If continued treatment of this type brings abatement of symptoms, *syphilis seems indicated, especially if* the radiologic evidence has disappeared and the patient is feeling better But unless the *T pallidum* is found in the lung tissue the diagnosis of pulmonary syphilis is not certain

## REFERENCES


FINDLAY C W JR LEHMAN W I and ROTTENBERG L H Gumma of the Lung Report of a Case Treated by Lobectomy Ann Surg 1949 *129* 274-84

KLUCHER G A and WINDHOLZ F Clinical Radiologic and Pathologic Aspects of Late Pulmonary Syphilis Effects of Penicillin Therapy Am J Syph 1947 *31* 166

LIBACH I M Syphilis of the Lung Brit J Vener Dis 1950 *26* 126

O LEARY R A and OCKULY O E Syphilis of the Lung Jour Lancet 1945 *65* 154

SMITH J W LAQUEUR G L and BARNETT C W Gumma of the Lung Proved by the Demonstration of Treponema Pallidum Am J Syph 1950 *34* 383


## PULMONARY FIBROSIS

Pulmonary fibrosis represents the reparative process following any injury to the lung parenchyma of sufficient severity to cause actual destruction of tissue Fibrosis has *long been recognized as the sequela of a wide* variety of diseases but our understanding of the underlying pathology has been extremely meager and for the most part, limited to quantitative rather than qualitative distinctions Recently Spain has called attention to the several distinctly different patterns of pulmonary fibrosis His studies indicate that the pattern and the distribution of the fibrosis are more closely correlated with the clinical manifestations than is the degree of the fibrosis

*Bronchiolar Fibrosis* —Various inflammatory processes among them acute and chronic bronchitis, diffuse bronchiolectasis, asbestosis phosgene poisoning and diffuse *endobronchial tuberculosis*, exert their primary destructive effect on the bronchi and bronchioles If the process is severe enough healing is associated with the *deposition of* sufficient fibrous tissue in and around the bronchiolar wall to produce narrowing of the lumina and obstructive emphysematous changes distally Since the basic pathology is usually diffuse the emphysema is characteristically generalized A significant reduction in vital capacity results and cor pulmonale is rather frequent

*Interstitial Fibrosis* —Certain diseases all of them rare tend to fibrosis of the interstitial tissue of the lung A classic example is idiopathic pulmonary fibrosis characterized by a startling degree of widespread hyperplasia of the interstitial connective tissue Similar changes are encountered in berylliosis in bauxite poisoning and occasionally, in scleroderma In contrast to bronchiolar fibrosis, the altered physiology here is respiratory not ventilatory for there is no emphysema or increase in the residual air but instead, a diminished $O_2$-$CO_2$ exchange due to fibrous deposition between the alveoli and pulmonary capillaries Decrease in the pulmonary vascular bed from fibrosis leads not infrequently to cor pulmonale

*Parenchymal Fibrosis* —This is the most *common type of pulmonary fibrosis* encountered It may follow a wide variety of diseases such as unresolved pneumonias (including Friedlander s) mycotic diseases of the lung tuberculosis silicosis pulmonary infarction radiation pneumonitis and lipoid pneumonia Both bronchial tree and lung parenchyma are *obliterated so that function* in the involved portion of the lung is completely lost Compensatory emphysema in the remainder of the lung is the normal sequence of events yet is generally not severe enough to cause symptoms Cor pulmonale does not usually occur

*Pulmonary Vascular Fibrosis* —Primary fibrosis of the pulmonary arterioles is uncommon most cases being secondary to the pulmonary hypertension accompanying generalized emphysema The increased resistance to blood flow through the pulmonary *bed places a strain on the right ventricle* a strain eventually leading to cor pulmonale

## IDIOPATHIC FIBROSIS

Idiopathic pulmonary fibrosis (diffuse interstitial fibrosis) is a rare pulmonary disease of a gradually progressive character associated with a tremendous amount of hyperplasia of the interstitial pulmonary connective tissue. The etiology is unknown but the disease is probably of virus origin. The clinical course is marked by severe dyspnea, chronic cough and cyanosis in association with minimal lung findings on physical examination. Death is inevitable for no satisfactory treatment has as yet been devised. However, it may be that the disease occurs in localized form; if so there must be many undiagnosed cases from which the patient recovers.

### REFERENCES

*Pulmonary Fibrosis*

SPAIN, D. M.: Patterns of Pulmonary Fibrosis as Related to Pulmonary Function. Ann. Int. Med. 1950 *33* 1150.

*Idiopathic Fibrosis*

BEAMS, A. J., and HARMOS, O.: Diffuse Progressive Interstitial Fibrosis of the Lungs. Am. J. Med. 1949 *7* 425.

HAMMAN, L., and RICH, A. R.: Acute Diffuse Interstitial Fibrosis of the Lungs. Bull. Johns Hopkins Hosp. 1944 *74* 177.

PEABODY, J. W., PEABODY, J. W., JR., HAYES, F. W., and HAYES, F. W., JR.: Idiopathic Pulmonary Fibrosis: Its Occurrence in Identical Twin Sisters. Dis. Chest 1950 *18* 330.

## PNEUMOCONIOSIS

Pneumoconiosis is largely an occupational disease since in most cases it results from prolonged inhalation of small particles of dust, usually silica, in the atmosphere of mines and industrial plants. It has been estimated that approximately 5 per cent of those who work in this country have been exposed to dust diseases; of these 10 per cent or about a fourth of a million workers have been affected. Silica dust, the chief agent in pneumoconiosis, is inhaled from the air by everyone, and at autopsy is found mottling the parenchyma of the lungs, the degree of mottling depending on the individual's degree of exposure to the dust (the lungs of coal miners, for example, are almost black). A mild pneumoconiosis exists unsuspected in many inhabitants of manufacturing cities where the atmosphere is filled with smoke and dust. A study made in Chicago in 1941 showed that on the average 55 tons of dust per square mile fell from the air each month. Dust storms may also cause considerable deposits of dust particles in the lungs. However these deposits are not disabling although they occasionally lead to acute bronchitis or to asthmatic attacks. It has been calculated that a worker must be exposed to silica dust for from 15 to 20 years and inhale between 15 and 20 million silica particles per cubic foot of air before pneumoconiosis is established.

Pneumoconiosis, which is manifested by a pulmonary fibrosis, not only is the cumulative effect on a susceptible worker of long exposure to silica dust in the atmosphere but is also dependent for its development on the size and composition of the silica particles and on the presence of other respiratory conditions before or during exposure to the atmosphere containing the particles. Since disease due to industrial dust is common and workmen's compensation laws and other legal aspects of the problem require accurate estimates of the degree of disability it causes, the injurious effect of industrial dust is of great concern to physicians. Medicine and industrial management are both trying to find ways to lower the concentration of industrial dust and make the dust itself innocuous to the worker.

Most of the affected workers are middle-aged men who have been employed continuously in a dust laden atmosphere and have gradually accumulated disabling masses of dust particles in their lungs. The illness may be precipitated by a concurrent pulmonary disease or by factors due to the aging process such as arteriosclerosis, cardiovascular disease, obesity, and skeletal changes. These factors must be taken into consideration both in treating the disease and in estimating the amount of disability of occupational origin. One employee, for example, may continue to work making light of a very real disability; another only slightly affected may become emotionally unfit to work. Diagnosis of pneumoconiosis is not simple and often requires expert scientific

study before liability of the employer can be determined

## SILICOSIS

Various nonsilicous inorganic and organic dusts cause either a pneumoconiosis or some other pulmonary affection but the inorganic dusts containing silica are responsible for most of the cases recognized as pneumoconiosis The symptoms of pulmonary fibrosis and its complications occurring in silicosis are typical of most other forms of the disease and in fact of pulmonary fibrosis resulting from any pulmonary affection

Silicosis occurs among workers in many industries, including sandblasting coal mining stone crushing sandstone industries metal grinding pottery-making tunnel building, the manufacturing of abrasive soaps and powders and metal mining

*Pathogenesis* —No form of pneumoconiosis can develop unless the individual is directly exposed to a dust laden atmosphere for a considerable length of time Furthermore not all workers so exposed will develop the disease A third important fact is that before they can be considered dangerous to health the dust particles must be small enough to enter the terminal bronchioles No particle more than 10 microns in diameter can enter the alveoli About 75 per cent of the particles found in the alveoli are less than 3 microns in diameter these are the most dangerous particles

Little of the dust that is inhaled reaches the lungs The narrowness of the nostrils the coarse nasal hairs that trap the dust as it is inhaled and the nasal secretions that wash out the dust particles serve as a protecting mechanism along with the ciliated epithelium of the trachea which with an escalator movement turns the inhaled particles back into the pharynx whence they are expectorated or swallowed

When the particles enter the alveoli the self-cleansing system is activated the phagocytes of the alveolar walls engulf the particles and deposit them in the lymph stream But the phagocytes and lymph channels soon become overloaded then the dust particles block the lymph channels and a series of "dust depots" are formed in the air spaces

As this obstruction in the lymph nodes increases with continued inhalations of dust the pulmonary surface is covered with lesions, the lymphatic vessels being surrounded by beadlike fibrous tissue These formations coalesce to form a massive fibrosis Necrosis and cavitation eventually develop as a result of the decreased blood supply following extensive fibrosis Emphysema is a usual complication but other conditions may develop, such as abscess, spontaneous pneumothorax, pulmonary artery thrombosis hemorrhage adhesive pleurisy, and atelectasis all conditions which follow in the wake of any extensive pulmonary fibrosis

Whether the fibrosis is due to a chemical change in the silica particle as Gardner and many others believe, or to an inflammation caused by the hardness and sharpness of the dust has not been proved * Mayer and Rappaport point out however, that, though the hardness of quartz dust causes inflammation the comparable hardness of emery dust does not The degree of fibrosis depends on the degree of silica dust accumulation, but once nodulization begins, it is progressive A tuberculous process develops in a great many cases

The pulmonary fibrosis of silicosis is not always nodular it may be diffuse Fibrosis following inhalation of silica dust in quarries mines and potteries or any sandblasting industry, tends to be nodular in type characteristic whorled nodules being scattered over the lungs Diffuse fibrosis is found in anthraco-silicosis siderosilicosis, and other mixed silicoses resulting from coal or ore mining or in the diatomaceous earth industry Dust granulomas occurring as the alveolar walls are thickened by infiltration of lymphocytes plasma cells, and giant cells and formation of a fibrous reticulum are not uncommon

Nodular fibrosis contrary to general opinion is less damaging than diffuse fibrosis even in the milder grades since even the slight thickening of the alveolar septa over

* The fibrous response to crystalline dusts (silica etc ) depends on their being piezoelectrically active For discussion of this hypothesis see Silas M Evans M D and Robert L Kascht M D The Pathogenesis of Silicosis The Penna Med Jr Vol 52 Number 14 November 1949 —EDITOR.

diffuse areas greatly diminishes the breathing surface whereas nodular fibrosis however extensive promotes a compensatory emphysema Hence in early cases of diffuse fibrosis the clinical symptoms are out of proportion to the roentgenologic findings *It is possible to distinguish between a tuberculosilicosis* and a silicosis with tuberculosis the former exhibiting the characteristics of silicosis and the latter those of tuberculosis but they may develop simultaneously

gross fibrosis resulting from chronic tuberculous infection This process extends over many years The tuberculous infection may occur early or in very rare cases not at all

The onset of the disease is insidious and symptomless and develops slowly over a *period of years The earliest symptom is* dyspnea on exertion a dyspnea that increases as the disease progresses Another symptom is a dry hacking and nonproductive cough Later as tuberculosis develops

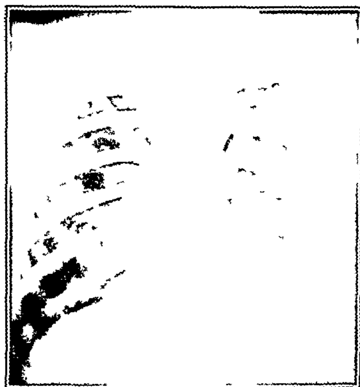


FIG 157 —Silicosis

the cough is accompanied by sputum mixed *with blood and is distressing* There is little pain unless pleurisy develops Chest examination reveals few if any signs at any time and those found are characteristic of any lung infection There may be a slight alteration of chest sounds with shortening of the inspiration phase and a few dry rales and later restriction of movement of the diaphragm and chest walls In the early stages of the disease radiographic examination shows only exaggeration of hilar markings but as the disease progresses shadows

In addition to the common tuberculous *complication of pneumoconiosis nonspecific* infectious complications may arise as a result of incompletely resolved bronchopulmonary lesions Recurrent infections may lead to pneumonitis and chronic abscess formation

*Symptoms and Diagnosis* —Three phases of silicosis have been differentiated (1) the bronchial phase characterized by dry bronchitis or bronchiolitis (2) the nodular phase characterized by small collections of lymphoid tissue in the lung and by fibrosis and (3) the infective phase, characterized by

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## SILICOSIS

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Little of the dust that is inhaled reaches the lungs. The narrowness of the nostrils, the coarse nasal hairs that trap the dust as it is inhaled, and the nasal secretions that wash out the dust particles serve as a protecting *mechanism along with the ciliated* epithelium of the trachea, which with an escalator movement turns the inhaled particles back into the pharynx, whence they are expectorated or swallowed.

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cinoma cardiovascular diseases scleroderma diffuse bronchiectasis adenomatosis and other pulmonary disorders Diagnosis depends on (1) known exposure to dust laden atmosphere over a long period, not necessarily recent (2) clinical symptoms and (3) x ray findings Tubercle bacilli must be present in the sputum before tuberculosis can be considered evident

*Treatment* —Treatment of silicosis is symptomatic only The worker should at once be removed from exposure to dust hazards But the disease will progress even after exposure to the causative dust has ceased The treatment of complicating diseases which should be prevented when possible is of immediate concern Mayer and Rappaport distinguish between therapy for tuberculosilicosis and therapy for silicosis with tuberculosis In the former the routine rest therapy employed in tuberculosis is not remedial nor is radical treatment feasible in the latter the treatment is that for active tuberculosis except that it must be more conservative

For impairment of pulmonary function in pneumoconiosis Motley recommends the simultaneous use of intermittent positive pressure breathing and nebulization of such bronchodilator drugs as vaponefrin and isuprel to promote bronchial drainage and relieve bronchospasm

The effectiveness of antibiotic therapy has not been demonstrated but when silicosis is accompanied by a purulent infection injections of penicillin and other antibiotics and aerosol inhalations are indicated Surgical drainage of pyogenic abscesses may be required The use of metallic aluminum has been employed chiefly as a preventive measure the aluminum presumably rendering silica particles nontoxic by forming an insoluble coating of gelatinous aluminum hydroxide around the particles to prevent their absorption

In the early phase of the disease attempts should be made through inhalation and injection of penicillin to prevent bronchial infections In the second or pulmonary phase ventilatory insufficiency is evident from the occurrence of dyspnea cyanosis on exertion emphysema tachycardia venous engorgement and cardiocirculatory embarrassment vaponephrin inhalation the administration of aminophyllin and penicillin and the wearing of an abdominal belt are advocated For the final or cardiac stage in which there is evidence of right ventricular failure and some orthopnea the use of digitalis mercuhydrin aminophyllin and periodic inhalations of oxygen are recommended When there is evidence of total heart failure use of positive pressure inhalation and phlebotomy may bring some relief

## ANTHRACOSIS

Anthracosis is a disease of coal miners and differs from silicosis in that the deposits in the lungs are pure carbon and the disability is caused by blockage of the air passages by these deposits Tuberculosis is uncommon in cases of anthracosis but anthracosis without silicosis is rare since the layers of coal lie between rocks containing much silica

## ASBESTOSIS

Asbestosis results from inhalation of asbestos and differs from silicosis in that the coarse nodular fibrosis common in silicosis does not develop there being a finer and more general distribution of fibrous tissue and therefore greater respiratory embarrassment Continuous dyspnea out of all proportion to the clinical and radiologic findings is a characteristic symptom Corns due to penetration of the skin by asbestos fibers may occur on the hands arms and legs and clumps of asbestos are found in the sputum The progress of the disease is slower than that of silicosis

## SIDEROSIS

Siderosis occurs among iron-ore workers metal-drillers and hemite miners Two types of siderosis are encountered the red and the black The first is due to iron oxide dust and occurs among employees in industries using iron pigments The lung tissues are hard and reddish with massive areas of fibrosis though almost no evidence of silicosis or tuberculosis The disease resembles anthracosis The black type of siderosis

indicating fibrous nodules with a tendency to coalesce may be observed, the outer and lower lung fields characteristically showing fewer nodules Generally, the presence of these shadows without an attendant dullness to percussion indicates a silicosis, if the shadows are present together with rales and dullness to percussion tuberculosis is indicated In the late stages of silicosis nodulation becomes more consolidated throughout the upper and midlung fields, liver may become enlarged and the tips of the fingers become clubbed Emphysema becomes increasingly evident, at first it is functional and compensatory but at last becomes structural Emphysema arises as the accumulations of dust particles cause fibrosis and loss of breathing area and force the reserve breathing surface to function With spreading of the fibrosis, this reserve breathing service is lost, and the emphysema is no longer compensatory



Fig 158 —Silico-tuberculosis

usually with associated emphysema Dyspnea and cough are now prominent and on exertion, there is cyanosis due to cardiac insufficiency due, in turn to interference with capillary circulation

The victim of the disease may work for years without evident distress or disability except for the increasing breathlessness With development of tuberculosis fever sweating hemoptysis decreased strength and loss of weight become evident The veins of the neck show engorgement the

When nonspecific infection is superimposed suppuration is also present in addition to fibrosis and emphysema In advanced cases of silicosis with suppuration symptoms of right heart failure become evident and indicate cor pulmonale If the patient does not die of tuberculosis he dies of pneumonia combined with pulmonary heart disease

Differential diagnosis is difficult since pneumoconiosis simulates so many other diseases as tuberculosis sarcoidosis car

cinoma cardiovascular diseases scleroderma diffuse bronchiectasis adenomatosis and other pulmonary disorders Diagnosis depends on (1) known exposure to dust laden atmosphere over a long period not necessarily recent (2) clinical symptoms and (3) x ray findings Tubercle bacilli must be present in the sputum before tuberculosis can be considered evident

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occurs among iron-workers and metal-grinders and polishers, and, since silica is usually present in the victims working atmosphere, silicosis and tuberculosis co-exist with the disease

## OTHER INORGANIC DUST DISEASES

New inorganic dust diseases are constantly being reported, diseases such as occur among workers in bauxite beryllium granite vanadium, *etc* The symptoms of these diseases differ little from those of silicosis

It has been shown that prolonged inhalation of chromate dust produces carcinoma of the lung Exposure to radon in uranium mines produces also malignancy of the lungs ( Schneeberger Lungen Krankheit ) (H Brieger)

## ORGANIC-DUST DISEASES

Diseases arising from exposure to organic dusts are not true pneumoconioses but should be considered here because of the pulmonary involvement Some of these inhaled materials contain fungi and living bacteria Anthrax bacilli may be inhaled by workers in processing hair furs or skins Fungi may be inhaled by those threshing grain

## SHAVER S DISEASE

Shaver s disease, named for its discoverer occurs among workers exposed to fumes from the electric furnace used in the production of fused aluminum The particles of aluminum are extremely small from 0 02 microns to 0 5 microns in diameter This is probably the reason for the very rapid development of the disease which causes profound pulmonary damage If death comes it comes in a few months whereas the silicosis victim lingers for years

## BERYLLIOSIS (*See* Chapter 13)

### REFERENCES

*Pneumoconioses Shaver s Disease*

Gardner L U Aluminum Therapy in Silicosis J Indust Hyg 1944 *26* 211

Gloyne S R *et al* Pneumoconiosis Due to Graphite Dust Thorax 1949 *4* 31

Greenberg Leonard, *et al* Pneumoconiosis Am J Pub Health 40 Pt 2 Yearbook 1950 149

Mayer Edgar and Rappaport Israel Pneumoconiosis Bantai A J Non tuberculous Diseases of the Lung Springfield Charles C Thomas *In press*

Motley H L *et al* Impairment of Pulmonary Function in Anthracosilicosis Arch Indust Hyg 1950 *1* 133

Riddell A R Clinical Aspects of Shaver s Disease Vorwald A J *Loc Cit* pp 459

Shaver C G Further Observations of Lung Changes Associated With the Manufacture of Alumina Abrasives Radiology 1948 *50* 760

Singer J J Differential Diagnosis of Chest Diseases Philadelphia Lea & Febiger 1949

Vorwald A J Pneumoconiosis New York Paul B Hoeber 1950

## THE PNEUMONIAS

Pneumonias due to bacterial and rickettsial agents have been discussed in Chapters 2 and 5 Only pneumonias due to the aspiration of certain materials or to miscellaneous causes are described here

### Aspiration Pneumonias

*Lipoid pneumonia* results from the aspiration of fatty substances such as mineral oil cod liver oil oily nose drops and milk Forced feeding of cod liver oil castor oil or mineral oil to crying children is no infrequent cause Although lipoid pneumonia occurs more often in children adults who commonly use nose drops may develop it Motor mechanics occasionally inhale fuel oil and machine workers oil from broken pressure lines both may develop lipoid pneumonia Vegetable oils are less irritating than animal oils the latter having a high fat content and being easily hydrolyzed Mineral oil is also less irritating than animal oils but may act as a foreign body and produce inflammatory changes

Roentgenologically the infantile type of lipoid pneumonia simulates atypical pneumonia In the adult the clinical symptoms in the later stages of the disease seem to indicate a chronic pneumonitis On $x$ ray the findings at first resemble those of the hepatization stage of lobar pneumonia then with the development of a dense fibrosis,

they may mimic those of a bronchogenic carcinoma Suspicion of a neoplasm may sometimes lead to a pneumonectomy where a lobectomy would have sufficed

### Miscellaneous Pneumonias

*Post irradiation pneumonia* is an infrequent sequel to irradiation therapy for breast cancer In the presence of such a cancer it may be difficult to decide whether the fibrosis present is due to the neoplasm or to the effect of the irradiation

Roentgenograms may reveal consolidation extending from the hilum into the lung fields and occasionally a pleural effusion These irradiation lesions may disappear spontaneously without leaving permanent damage The symptoms of post irradiation pneumonia—cough irregular periods of fever and dyspnea—simulate those of chronic pneumonitis

### Chemical Pneumonitis

Exposure to a great number of irritating gases such as nitrous oxides sulphur oxides fluorides and others may produce chemical pneumonitis as was observed in the Donora episode (H Brieger)

#### References

*Pneumonias*


Berg R Jr and Burford T H Pulmonary Paraffinoma (Lipoid Pneumonia) J Thoracic Surg 1950 20 418 (Discussion by J J Harter)

Cannon P R Problems of Lipid Pneumonia J A M A 1940 115 2176

Leach J E Abnormal Pulmonary Physiology as a Result of Chronic Irradiation Pleuropneumonitis Am J Roentg 1943 50 772

Losner S et al Diagnosis of Lipoid Pneumonia by Examination of the Sputum Am J Clin Path 1950 20 539


## ALLERGIC PNEUMONIA LOEFFLER'S SYNDROME

Loeffler's syndrome is characterized by transitory migratory parenchymal infiltrations mild pulmonary symptoms a high blood eosinophilia and uneventful clinical course and spontaneous resolution Its etiology is uncertain It is frequently observed in asthmatic or allergic individuals A tuberculous origin seems unlikely since tuberculin tests may be either positive or negative Since parasites are not infrequently found in cases of this disease a parasitic origin for it has been given some credence The allergic theory of its origin however has received most support

#### References


Bantal A I and Peabody J W Nontuberculous Diseases of the Chest Springfield Charles C Thomas In Press

Peabody J W Transitory Migratory Pulmonary Infiltration Associated with Eosinophilia Dis Chest 1944 10 391


## MYCOTIC DISEASES OF THE LUNG

The mycoses are discussed elsewhere in detail but because of the frequency with which pulmonary mycosis occurs points pertaining to mycotic lung involvement deserve special comment (*See* Chapter 9)

Actinomycosis —Primary pulmonary actinomycosis is usually bilateral and involves especially the lower lobes although no location is necessarily spared so that tuberculosis bronchogenic carcinoma or almost any other condition may be mimicked Early cases are characterized by a mild type of respiratory infection with low grade fever cough and varying amounts of mucoid sputum which later becomes thick purulent and sometimes blood streaked The initial lesions subsequently show abscess formation and extension to the pleura and thoracic cage together with the development of draining cutaneous fistulas Pleural involvement leads to thickening of the pleura pleuritic pain and occasionally effusion In untreated or unresponsive cases signs of a chronic debilitating disease eventually appear together with clinical and laboratory evidence of a severe infection Deformities of the chest wall may result

X rays of the chest usually reveal extensive patches of consolidation usually bilateral and involving the bases Fan shaped masses radiating from the hilum may be encountered More uncommon are apical

lesions resembling those of the active reinfection type of tuberculosis. The mediastinum becomes distorted in advanced cases, and pleural and rib involvement are frequently demonstrable.

The demonstration of typical "sulfur granules" or mycelial filaments in the sputum or in the pus from draining sinuses is generally diagnostic, but it should be remembered that pathogenic strains of *A. bovis* constitute a common contaminant of the gums and saliva of normal individuals. A biopsy of the wall of a draining sinus may show granules when none are present in the drainage.

NOCARDIOSIS.—Increasing attention is now being devoted to nocardiosis because of its strong clinical resemblance to tuberculosis. It is the general impression that the disease is much more frequent than its rate of diagnosis would indicate. The picture is primarily that of pulmonary involvement, with signs and symptoms that are, at first, mild and similar to those of bronchitis with unproductive cough, low grade fever, and vague chest pain. Even as the disease progresses, the patient does not appear as sick as the radiographic evidence would indicate. Empyema is a frequent complication, and fistulous tracts similar to those with actinomycosis are apt to occur in chronic cases. Hematogenous spreading accounts for involvement of other organs, especially those of the central nervous system; metastatic brain abscesses occur in about 25 per cent of cases. The lower lung fields again appear to be somewhat more often affected, but apical lesions are by no means uncommon. Certainly in any obscure lung disease suspected of being tuberculosis, nocardiosis should be considered when tubercle bacilli cannot be found. Of interest here is the fact that the method of concentrating sputum for acid fast studies actually destroys *N. asteroides*.

COCCIDIOIDOMYCOSIS (SAN JOAQUIN VALLEY FEVER).—Coccidioidomycosis follows inhalations of dust containing the spores of Coccidioides immitis and, in the vast majority of cases, is limited to an acute infection of the upper respiratory tract. This infection is benign and generally mild or even subclinical, occasionally it is severe. By skin testing with coccidioidin, it has been shown that, in the endemic areas, most of the inhabitants have been previously infected with the primary pulmonary type of coccidioidomycosis. Chest pain accompanies most cases, usually, it is substernal and aggravated by respiration or cough. Cough, chills, and fever, headache, sore throat, and general malaise are other frequent complaints. Some stress the occurrence of substernal pain on swallowing as a peculiar but highly suggestive feature in about 25 per cent of the cases. Allergic skin manifestations, such as erythema nodosum or erythema multiforme accompany about 5 or 10 per cent of the cases. Hemoptysis is very infrequent at this stage. Physical findings are variable. On x ray examination the majority of cases exhibit a fairly well-defined homogeneous density radiating peripherally in fan shaped fashion from the hilum. Discrete nodular lesions in the periphery are less common but are typical of the disease and probably represent an unresolved infiltration of the former type. Peribronchial infiltration and hilar and mediastinal adenopathy are frequent associated *findings and may constitute the only evi*dence of the disease. The lower lung fields are much more frequently involved, but in some cases apical reinfection tuberculosis may be closely simulated. Complete recovery can be anticipated in from 6 to 8 weeks, *but, in a small percentage of cases* characteristic thin walled cavities may persist. These are usually apical (70 per cent) and may close spontaneously (if small) or cause no subjective complaint. In a few cases, however, recurring hemoptysis with persistent or giant cavitation eventually necessitates pneumothorax, phrenic crush or even lobectomy for cure. Before any such decision, refractoriness to a therapeutic trial of bed rest should be demonstrated, most authorities feeling that the therapy for primary pulmonary coccidioidomycosis is in this respect essentially the same as the therapy for tuberculosis. On the other hand one should recall that the sputum of those with coccidioidomycosis is never infectious, for it contains only endospores which are not infective.

In about 1 case in 100 the primary form goes into progressive coccidioidomycosis then the course becomes chronic the disease systemic and the prognosis extremely dark Respiratory symptoms and fever persist and are joined by generalized weakness and wasting as well as by symptoms from bone joint cerebral and visceral spread Negroes Mexicans and Filipinos appear to be particularly susceptible The mortality rate for the progressive type of the disease is over 50 per cent

HISTOPLASMOSIS (DARLING'S DISEASE) — Men are affected twice as often as women Recent skin testing surveys with antigen derived from cultures of *H capsulatum* have revealed a startling degree of past infection among inhabitants of endemic areas It is felt that there is a benign type of histoplasmosis similar to that of coccidioidomycosis a type characterized by a subclinical or mild clinical course from which recovery is complete Sensitivity to histoplasmin and the presence of small pulmonary calcifications indistinguishable from healed tuberculous lesions are the only residua of the disease There are astonishingly few instances of the progressive systemic form of the disease Symptoms include dry cough weakness dyspnea chills and fever night sweats chest pain and occasionally hemoptysis Weight loss is often marked Chest x rays may show anything from increased bronchovascular markings to areas of pneumonitis The classical mycotic picture of fan like hilar radiations occurs in only a third of the cases Miliary studding of both lung fields occurs in snowstorm fashion despite the negligible incidence of apical involvement

In the overall picture the lung findings play a very small part in comparison to the hepatomegaly splenomegaly lymphadenopathy and marked inanition which accompany visceral histoplasmosis Leukopenia and anemia occur as a result of bone marrow destruction The progressive form of the disease is almost universally fatal

NORTH AMERICAN BLASTOMYCOSIS (GILCHRIST'S DISEASE) — Though a great many primary benign forms of coccidioidomycosis and histoplasmosis have been demonstrated in recent years no such corresponding variety of forms has been discovered for blastomycosis Nearly all systemic cases are fatal progressing from a mild respiratory infection to extensive lung involvement In the early stages a dry nonproductive cough chest pain and low fever occur purulent blood streaked sputum dyspnea and high fever come later General debility ensues and night sweats may become particularly severe In most instances there is concomitant skin involvement Subcutaneous abscess formation with subsequent cutaneous fistulas is rather typical

MONILIASIS — Bronchopulmonary moniliasis is not uncommon but in many instances is never diagnosed as such The signs and symptoms are those of chronic bronchitis— chiefly a persistent cough productive of gray flecked mucoid sputum containing budding yeastlike cells The course is mild and chronic and roentgenograms reveal little more than a slight peribronchial infiltration

ASPERGILLOSIS — Pulmonary involvement in aspergillosis is uncommon but when it occurs often shows a marked similarity to that in tuberculosis

CRYPTOCOCCOSIS (TORULOSIS) — The *Cryptococcus neoformans* has a predilection for the central nervous system and to some degree the lungs In fact the organism is thought to gain entrance via the respiratory tract where it causes a mild infection characterized by persistent cough and low fever Any portion of the lung may be involved

GEOTRICHOSIS — There are a number of types of *Geotrichum* which cause geotrichosis and all are frequent contaminants The most frequent form of the disease is bronchopulmonary but in most instances the only symptom is a persistent and harrassing cough productive of a small amount of mucoid sputum

A pulmonary form of the disease also exists but is much less common It is characterized by a systemic reaction with fever leucocytosis purulent sputum and occasional hemoptysis a picture not unlike that of tuberculosis

SPOROTRICHOSIS — Pulmonary forms of this disease rarely occur for it involves primarily the lymphatic system and other systems of the body When it does occur it presents the picture of a low grade pulmonary infection

## BIBLIOGRAPHY

*Mycotic Diseases of the Lung*
*General*

ANDOSCA J B and FOLEY J A Fungus Disease of the Lungs Postgraduate Med 1949 *6* 443
ASH J E and SPITZ S Pathology of Tropical Diseases An Atlas Philadelphia W B Saunders Co 1945
CONANT N F MARTIN D S SMITH D T BAKER R D and CALLAWAY J L Manual of Clinical Mycology Philadelphia W B Saunders Co 1945
HOBBY A W Pulmonary Mycoses Dis Chest 1949 *15* 174

*Actinomycosis*

POPPE J K Treatment of Pulmonary Actinomycosis with a Report of Seven Arrested Cases J Thor Surg 1946 *15* 118

*Nocardiosis*

HAGER H F MIGLIACCIO A V and YOUNG R M Nocardiosis Pneumonia and Empyema Due to Nocardia Asteroides New Eng J Med 1949 *241* 226

*Coccidioidomycosis*

ARONSON J D SAYLOR R M and PARR E I Relationship of Coccidioidomycosis to Calcified Pulmonary Nodules Arch Path 1942 *34* 31
BERKE R SCHOMER A and BOSS H E Residual Cavities in Pulmonary Coccidioidomycosis Follow Up Studies Dis Chest 1950 *17* 84
COTTON B H and BIRSNER J W Surgical Treatment in Pulmonary Coccidioidomycosis J Thor Surg 1950 *20* 429
NORMAN I L and LAWLER A I Coccidioidomycosis Review of the Literature and Report of 9 Case U S Nav Med Bull 1949 *49* 1005

*Histoplasmosis*

HODGSON C H WEED L A and CLAGETT O T Pulmonary Histoplasmosis Review of Published Cases and Report of an Unusual Case J Thor Surg 1950 *20* 97

*Blastomycosis*

FELD D D and CADDEN A V Systemic Blastomycosis Dis Chest 1949 *16* 473

*Moniliasis*

FARRELL W A Bronchomoniliasis Canad M A J 1943 *48* 28
HIATT J S JR and MARTIN D S Recovery From Pulmonary Moniliasis Following Serum Therapy J A M A 1946 *130* 205
MIALS J B Candida Albicans Infection Confused With Tuberculosis Arch Path 1943 *35* 427

*Aspergillosis*

GERSTL B WEIDMAN W H and NEWMAN A F Pulmonary Aspergillosis Ann Int Med 1948 *28* 62
SCHNEIDER L V Primary Aspergillosis of Lungs Am Rev Tuberc, 1930 *22* 267

*Cryptococcosis*

REEVES D L, BUTT, E M, and HAMMACK R W Torula Infection of the Lungs and Central Nervous System Arch Int Med 1941 *68* 5

*Sporotrichosis*

FORBUS W D Pulmonary Sporotrichosis Am Rev Tuberc 1927 *16* 599
SINGER J J Pulmonary Sporotrichosis Am Rev Tuberc 1928 *18* 438


## DISEASES OF THE PLEURA

Pleurisy, or pleuritis, is a commonly occurring inflammation of the pleura and may be primary or secondary acute or chronic A primary pleuritis which occurs but rarely is blood borne from a distant focus of infection A pleural inflammation may affect only a circumscribed portion of the serous membrane or involve the entire surface of the pleura According to the characteristics of the inflammatory exudate the pleurisy is designated *fibrinous* or plastic (dry), *serofibrinous* (wet) or *purulent* (empyemic) These three types of pleurisy really represent different stages of the same pathologic process and sometimes cannot be clearly differentiated from one another

*Fibrinous Pleurisy —Etiology* —Pleural inflammation usually results from infection by direct or lymphatic extension most often from the lungs but may extend from other thoracic structures such as the pericardium vertebra or any organ beneath the diaphragm The common etiologic agents are tubercle bacilli streptococci pneumococci staphylococci and viral and other pathogenic agents Inflammation of the pleura may occur in such conditions as rheumatic fever brucellosis tularemia fungous infections disseminated lupus erythematosis Pick s disease diabetic coma dehydration and uremic states trauma pulmonary infarction irradiation pneumonitis and neoplastic diseases Also the terminal stage of various chronic and debilitating diseases may be attended by an associated pleurisy

*Pathology* —The fibrin may be absorbed and the appearance of the pleura remain unchanged or the pleural membrane may permanently lose its glistening appearance and become thickened by the inflammatory

exudate which deposits fibrin on the pleural surfaces and brings about the formation of firm fibrinous adhesions that glue the two pleural surfaces together The process may stop at this stage or progress to the secondary stage in which a copious exudation of serum takes place

*Symptoms and Signs* —The first clinical manifestation of the disease may be a sudden sharp pain a pain increased by bending toward the uninvolved side and diminished by supporting the affected side The pain may be aggravated by breathing or may be present only on deep breathing or coughing The patient may be seen lying on the affected side and attempting to restrain movements of the chest to lessen the pain and distressing cough This tends to increase respiratory embarrassment and may increase dyspnea arising from pulmonary compression and decrease of vital capacity

The physical signs depend to a large extent upon the amount of fibrinous exudation In some patients there may be little or no characteristic signs except a to-and-fro friction rub heard over the lower lateral portions of the chest This is a characteristic sign but is absent in some cases On the other hand there may be restricted movements of the chest on the affected side abdominal breathing occasionally a weak unproductive cough chills and fever The diaphragm may be elevated in cases of a pronounced fibrinous exudation and the percussion note may be dull There is local tenderness which may be aggravated by the pressure of the stethoscope Breath sounds are diminished on the affected side and intensified on the uninvolved side Roentgenographic examination may show nothing abnormal in the early stages of the disease but after the pleura has become thickened a band of uniform density with a sharply defined inner margin may be noted between the lungs and ribs When there is an underlying pulmonary process the evidence of pleurisy is obscured unless tuberculosis is present in which case *x* ray findings of tuberculous lesions at the apex may cause pleurisy to be suspected

*Diaphragmatic Pleurisy* —Pleurisy may develop in the serous lining of the upper surface of the diaphragm without involvement of any other part of the pleura It is usually fibrinous in nature but may occasionally be serous or even purulent The resulting pain will not be located over the inflamed area but referred to the shoulder or to the abdominal region according to the part of the diaphragm affected The central segment of the diaphragm receives its nerve supply from the phrenic nerve infection in that area will produce a referred pain in the supraclavicular region of the shoulder The peripheral rim of the diaphragm is supplied by the lower six intercostal nerves, inflammation in that region causes referred pain in the abdomen The pain which is generally increased on deep breathing or coughing may be mild or if the pleurisy is acute recurrent sharp pains may occur attended by eructation of gas and vomiting Cough is frequently present and dyspnea pronounced The abdomen may be rigid and boardlike but usually is not sore on pressure Percussion sounds are usually negative but friction rub is occasionally heard in the diaphragmatic region

Adhesions are found between the diaphragmatic surface of the pleura and the diaphragm either at its periphery or at the costophrenic or mediastino-phrenic angle or may arise from the mediastinal surface of the lung connecting that surface of the pleura with the diaphragm or with the pericardium Differential diagnosis may be confusing In some cases perforating peptic ulcer appendicitis or gall bladder disease has been diagnosed and this has led to abdominal operation Radiologic examination however may reveal a shadow in the dependent portion of the thorax and flattening and immobility of the diaphragm Tenderness on deep pressure should suggest abdominal disease its absence is suggestive of diaphragmatic pleurisy The white blood-cell count is elevated in all these diseases

*Treatment* is the same as in other types of pleurisy —use of a binder on the abdomen to splint the affected area and application of an ice pack to relieve pain

*Serofibrinous Pleurisy* —Serofibrinous (wet) pleurisy frequently follows fibrinous pleurisy although the dry stage may not have been recognized The wet stage is due to exudation of thin serous fluid into the

pleural cavity. The physical signs will depend on the amount of effusion present and the mobility of the mediastinum. Usually there is an impairment of respiratory movement on the affected side and obliteration of the intercostal depressions over the site of the fluid. Respiratory fremitus is absent and the percussion note is usually flat over the fluid but may be tympanitic or Skodiac above that level. The line of dullness on percussion may assume an Ellis S-curve, with the highest curve in the axilla changing position with posture. The heart, trachea, and mediastinal contents may be displaced contralaterally. With effusion on the right side the liver dullness may be depressed below the costal margin.

Laboratory examination of the fluid will show that it has a specific gravity of 1.018 or more and a high albumin content; the presence of leukocytes will also be noted. Blood, chyle, or cholesterol crystals may be present and suggest the character of the primary lesion. Bacteriologic study will reveal the nature of the inflammatory agent. Fungi are only rarely found in the pleural exudate. A search should be made for tuberculosis if a large percentage of lymphocytes are present. A bloody exudate should suggest malignancy.

Roentgenologic studies before development of fluid or thickening of the pleura takes place may yield few findings beyond restriction of diaphragmatic movements on the involved side. To be visible from 300 to 400 cc. of fluid must usually be present, although a lateral *x* ray, with the patient prone, may reveal a smaller quantity.

Whereas a simple pleuritis may be of short duration, a serofibrinous pleurisy *heals slowly*. *As the effusion gradually* diminishes fibrous adhesions, as part of the healing process, obliterate part of the pleural space. If the exudation becomes purulent, however, the exudate is not absorbed and an empyema develops so that healing cannot take place until the pus is removed. Occasionally a bronchopleural fistula develops allowing the pus to escape through the bronchus.

A serofibrinous pleurisy may heal within a few weeks or may last for months, depending on its severity and on the treatment used. In from 70 to 80 per cent of the cases the pleurisy is of tuberculous origin and unless this is recognized and treated, manifest pulmonary tuberculosis will be noted in from 40 to 50 per cent of the cases within 5 or 6 years. On the other hand, if patients with tuberculous pleurisy are hospitalized for a period of 6 months, pulmonary tuberculosis *will develop in approximately only* 10 per cent of the cases.

Tubercle bacilli frequently invade the pleura usually within 3 to 6 months of a primary infection or during post-primary hematogenous dissemination and produce a tuberculous pleurisy. Tubercle bacilli may appear first in the pleura, the development of pulmonary tuberculosis being secondary. *In these cases, whether fibrinous or serofibrinous*, scar tissue may develop to bind the pleural surfaces together, thus promoting healing. When tuberculosis of the lung is known to be present, diagnosis of a pleurisy is not difficult, but when the presence of tuberculosis is not recognized diagnosis may be difficult. If the pleurisy is of the dry type the only evidence of tuberculous infection may be a low grade fever, and the diagnosis is usually not made until evidence of the tuberculosis is produced.

*Diagnosis.* — The clinical diagnosis of serofibrinous pleurisy can usually be made on a basis of (1) a history of increasing dyspnea following thoracic pain or discomfort, (2) careful physical examination, thoracentesis, and laboratory tests, and (3) confirmation by means of fluoroscopic and radiographic examinations. Small pleural effusions are elusive on examination and are often overlooked. X ray studies are therefore necessary for the detection of small, encapsulated, or atypically located effusions.

Aspirated fluid provides the only absolute evidence of a pleural effusion.

The laboratory examination of the fluid may show a normal leucocyte count or a slight lymphocytosis. *Examination of a* tuberculous effusion shows a characteristic straw-colored, thin or cloudy fluid having a specific gravity of 1.018 or more and a high albumin content. The fluid may contain a number of red blood cells and 70 per cent or more lymphocytes. Bacteriologic study should always be made. Culture of the fluid

may be negative even when the presence of tuberculosis is known and repeated cultures may be required In doubtful cases recourse may be had to the tuberculin test A fungous infection is seldom found When the percentage of lymphocytes is high a test for tuberculosis should invariably be made preferably by guinea pig inoculation If the exudate is bloody malignancy should be considered

There are two diagnostic problems therefore in suspected serofibrinous pleurisy (1) differentiation between this type of pleurisy and conditions producing similar appearances (thickened pleura pneumonia new growths the empyemas hydrothorax atelectasis pericarditis with effusion and subdiaphragmatic conditions such as echinococcus of the liver abscess of the liver and subphrenic abscess) and (2) identification of the causative microörganism

*Treatment* — The treatment of pleurisy is directed to relief of pain and pressure symptoms Bed rest is fundamental in order to treat the underlying disease successfully In dry pleurisy bed rest alone may bring recovery Salicylates barbiturates codein heat adhesive strapping and counter irritants have all been recommended for dry pleurisy When the pain is severe injection of procaine solutions into the skin above the affected area or into the pleura brings relief Diffuse pain is sometimes treated with intercostal nerve block by injection of a 1 per cent procaine solution Resolution or organization of the initiating disease brings about subsidence of symptoms

When the amount of fluid is profuse aspiration may be necessary to relieve the dyspnea and pressure symptoms but aspiration should be delayed until the very acute febrile stage has passed unless the dyspnea becomes severe When aspiration is done early in the course of the disease the fluid re accumulates rapidly If allowed to remain unaspirated for a number of weeks pleural thickening may develop with permanent damage to respiratory function On the other hand if tuberculosis is present fluid removal may allow too rapid re-expansion of the lung and make the condition worse Only enough fluid should be aspirated to relieve the dyspnea as the remainder tends to be absorbed spontaneously if not aspiration should be repeated The fluid should be aspirated as much as possible before signs of cardio-respiratory distress develop If the patient complains of a pulling sensation in the chest is dyspneic or is coughing slightly thoracentesis must be stopped at once for these symptoms are an indication of too rapid re-expansion of the collapsed lung or of a shifting mediastinum and show that therefore a torsion of the great vessels at the base of the heart is threatened A small amount of air introduced will bring symptomatic relief and permit satisfactory radiologic and fluoroscopic determination of the site of the fluid Replacement of fluid by air is contraindicated in nontuberculous pleurisy and care should be taken by means of a check valve apparatus to prevent the entrance of air Before withdrawing the aspirating needle from 50 000 to 100 000 units of penicillin in 50 cc of saline solution may be introduced into the pleural cavity through the same needle in order to prevent infection But if the bacteriologic examination has revealed penicillin resistant organisms streptomycin (not to exceed 10 000 units per cc ) may be substituted If the effusion is tuberculous use of streptomycin is not recommended

A pneumothorax may be performed at the time of thoracentesis only if there is radiologic proof of the presence of pulmonary tuberculosis If a pneumothorax is done it should be performed before adhesions form otherwise an empyema may follow

*Pleural calcification* is rather uncommon and results from a tuberculous pleurisy or empyema pleural hematoma or hemothorax Physical signs of thickening of the pleura may indicate a fibrosis rather than a calcification When associated with an active tuberculous empyema calcification becomes serious for it acts as a foreign body and prevents healing and also by causing rigidity of the pleura prevents collapse of the cavity by thoracoplasty Diagnosis is made radiologically No treatment is given unless complications demand radical removal of the calcified parts of the pleura and complete thoracoplasty

## Empyema

*Etiology.*—Empyema, or pus in the pleural cavity, seldom if ever, occurs as a primary disease. Usually, it is secondary to an intrapulmonary infection, such as pneumonia, bronchiectasis, pulmonary abscess, pulmonary mycosis, or tuberculosis, or to a mediastinal or pericardial infection. Occasionally it results from stab wounds of the chest or rupture into the pleural cavity of mediastinal or subphrenic abscesses. The bacterial organisms most frequently found in empyema are pneumococci, streptococci, staphylococci, and tubercle bacilli.

The empyema usually forms over the site where the pneumonic process encounters the pleura and, in recumbent patients, tends to form in the posterior part of the chest. Undiagnosed and untreated, the empyema may burrow through the lung to a bronchus, or it may form "nests" in the parenchyma.

*Clinical Features.*—The symptoms of empyema are usually clouded by those of the primary disease but are increased by the inflammatory effect of the fluid formation on the parenchyma. In an extensive empyema the usual signs of pleural effusion are produced—dullness to percussion and immobility on one side of the chest, displacement of the heart away from the affected side, diminution of breath sounds and vocal fremitus over the affected area with tubular breathing above. These signs will be absent in small empyemas and the diagnosis delayed. Nevertheless, even if the quantity of fluid is small, limitation of respiratory motion may be noted.

X-ray studies may be helpful in the diagnosis but diagnosis cannot rest upon these findings alone, since similar shadows are caused by various collections of fluid in the lung. Aspiration will produce a thin, grayish fluid in early cases; later this becomes a thick, creamy pus which microscopically shows a high polymorphonuclear cell count. Laboratory studies will reveal the types of bacteria present. As the disease progresses the pus becomes very foul, indicating a mixed infection and the probable presence of a bronchopleural fistula.

Large accumulations of pus may erupt spontaneously through the chest wall (empyema necessitatis). A chronic empyema may develop from an acute empyema if the latter is untreated. In some instances, the patient may continue to work without discomfort with a large mass of pus in the chest. Eventually a gradual loss of weight, cough, and pain in the chest may cause him to seek a physician, and a suspicion of tuberculosis may be aroused.

Empyema may be distinguished from a serofibrinous pleurisy by its history of a preceding pneumonia and the bacteriologic findings. It is differentiated from pneumonia by the great toxicity present in empyema. Differentiation from pulmonary abscess is made on the patient's history, for the abscess usually follows an operation or aspiration of a foreign body; also, the abscess is rarely so extensive as an empyema becomes. Laboratory studies of the fluid, together with the patient's history, will distinguish between a tuberculous and a nontuberculous empyema.

*Treatment.*—Treatment of empyema is based on adequate drainage of the infected pleural cavity, elimination of organisms, obliteration of the empyema cavity, and reexpansion of the lung. Since the advent of the antibiotics, the treatment of empyema may be medical only, and early therapy may now be expected to bring recovery. Surgical intervention can be delayed with safety for one or two weeks, until it can be determined whether antibiotic treatment with aspirations will be successful.

A complete aspiration of the fluid daily and cleansing of the cavity with from 50 to 100 cc. of isotonic saline solution containing 1000 units of penicillin per cc. is advised. Even if operative drainage seems inevitable, preoperative antibiotic instillations may help to bring about localization of the empyema and prevent massive collapse of the lung. Empyema due to Gram-positive organisms requires treatment with penicillin, whereas those due to Gram-negative organisms or tubercle bacilli require streptomycin or other antibiotics. They should be given systemically and by instillation into the pleural cavity. They may be administered singly or together. Supportive treatment to maintain a satisfactory nutritional state is

important in either medical or surgical therapy

Improvement may be striking within 48 hours Aspiration of fluid and irrigation must be done daily When the exudate becomes sterile intrapleural antibiotic therapy can be discontinued and aspiration performed only when the fluid has not been reabsorbed Parenteral administration of the antibiotic should be continued until the temperature has been normal for a period of 3 days or more The aspiration of fluid must be complete each time it is attempted Daily x ray and fluoroscopic studies are advised during this period

Antibiotic therapy may suffice in empyema necessitatis Chronic empyema particularly when due to anaerobic bacteria will usually require operative drainage or pleural decortication

Recently the catalytic and enzymatic properties of streptokinase and streptodornase in promoting hydrolysis of fibrin and pus have been recognized Lysis of the pus in empyema following injection of these agents permits removal of the exudate by thoracentesis or by closed drainage through a thoracotomy tube They prevent further bacterial infection and promote closure of the cavity and healing

## Pneumothorax

*Etiology* —Pneumothorax is an accumulation of air or gas in the pleural cavity It follows a wound in the chest spontaneous rupture of the visceral pleura caused by underlying disease or artificial induction for diagnostic or therapeutic purposes Spontaneous pneumothorax once considered almost always due to a pulmonary tuberculosis is usually caused by rupture of emphysematous blebs asthma or rupture of a lung abscess It may be secondary to mediastinal emphysema (*see* page 957)

Spontaneous pneumothorax is of several types the closed type with small variations in intrapleural pressure causing mild symptoms the open type with atmospheric pressures due to communication with the bronchial tree causing moderately severe symptoms the tension or valvular type permitting inspiratory ingress of air and causing alarming symptoms due to highly positive intrapleural pressure Spontaneous pneumothorax of unknown etiology may occur in an apparently healthy individual It is usually observed in persons between the ages of 20 and 40 and more frequently in men than in women It is sometimes reported in the newborn and very young infants

*Pathogenesis* —The immediate cause of a spontaneous pneumothorax may be some act of the patient—heavy lifting sudden twisting of the body severe coughing or straining at stool Often the patient cannot recall any precipitating act He may have been lying in bed

When rupture of the pulmonary tissue takes place air escapes into the pleural cavity If the lung becomes completely collapsed there will be a shift of the heart and mediastinum toward the opposite side The edges of the tear may become sealed by the fibrinous effusion which follows no further air escapes and the lung gradually re-expands If the edges of the tear are held apart by adhesions on one side and by the collapsing lung on the other the gap may remain open The collapsed lung may become atelectatic in time the lung becomes permanently unable to re-expand When the opening becomes valve like so that there is an increasing escape of air into the pleura without release in the opposite direction a tension pneumothorax develops

Pneumothorax may be recurrent Coughing may cause a new separation of the healed edges of the hole and allow air to escape again into the pleural cavity With each coughing spell more and more air will be trapped and the mediastinum and heart further displaced In some instances the excessive tension may cause downward displacement of the diaphragm and if high enough may ultimately bring about a herniation of the pleural space rupturing into the mediastinum or even into the opposite pleural cavity Bilateral pneumothorax may occur if complete death will ensue Sometimes the pneumothorax will alternate from side to side

Little or no effusion occurs in simple benign pneumothorax However if there is underlying tuberculosis and the pleura becomes infected with tuberculous exudates a

clear serous effusion forms causing a hydropneumothorax; if there is pus, a pyopneumothorax results. The former is more common in the course of tuberculosis and the latter in suppurative conditions, such as lung abscess.

*Clinical Features.*—The symptoms of pneumothorax vary according to whether the onset is sudden or insidious, the amount of air that has accumulated in the pleural space and the general condition of both the affected and unaffected lungs. The pneumothorax may produce few symptoms until the accumulated air causes an alarming climax. The patient who has been unaware of more than a vague discomfort in his chest may, upon exertion, become dyspneic and, for the first time, consult a physician. In sudden onset, a sharp pain in the chest, upper abdomen or back, tightness in the chest, acute dyspnea, marked cardiac palpitation and a feeling of suffocation may follow a sensation of something's having snapped in the chest. These symptoms may subside if the escape of air into the pleural cavity ceases and compensation takes place by depression of the diaphragm and shifting of the mediastinum and heart toward the other side. If the tension should increase, preventing return of blood to the heart, the patient becomes cyanotic and may die of asphyxia and cardiac failure.

The physical signs also vary according to whether the pneumothorax is complete or partial, the condition of the affected lung and the fixity of the mediastinum. In partial pneumothorax diminished expansion is noted on the affected side. The percussion note is hyperresonant and voice sounds are diminished or absent on the affected side. Breath sounds are absent or diminished on that side and exaggerated on the opposite side if the healthy lung is over-expanding in compensation. In complete pneumothorax the signs are more striking with immobility of the chest and absence of both breath and vocal sounds, and a tinkling coin sound may be heard. A pericardial knock may be noted in a left sided penumothorax without fluid. Shaking the body when fluid is present produces a pathognomonic succussion splash. The larger the hole, the deeper are the amphoric breath sounds.

If a tension pneumothorax develops, a widening of the intercostal space on the affected side can be observed with obliteration of the intercostal depressions. The chest on that side becomes immobile and the chest wall appears smooth and bulging, the trachea and the apex of the heart are usually displaced toward the other side. The percussion note becomes hyperresonant or tympanitic. Voice and breath sounds are not heard. Occasionally, as the tension gradually increases, the diaphragm is lowered and liver dullness is depressed. Tachycardia and arrhythmias may give evidence of marked displacement of the heart and mediastinum.

Roentgenologic examination is necessary to determine the degree of collapse of the lung.

*Diagnosis.*—If the pneumothorax is only partial, the slight attending pain may be overlooked or be regarded as pleurisy. When more complete, the severe pain accompanied by dyspnea may be mistaken for perforation of a peptic ulcer or cardiac infarction. Large pulmonary cavities and diaphragmatic hernias or a congenital cyst may simulate a pneumothorax and differentiation may be difficult.

*Treatment.*—Therapy is largely symptomatic in patients with an open or closed spontaneous pneumothorax uncomplicated by an underlying infection. Quiet bed rest, sedatives for relief of pain and careful watching for development of a valvular mechanism in the tear are necessary, with reassurance of the frightened patient. Frequent roentgenographic and fluoroscopic examinations should be made to determine progress of the disease. Control of cough will help to prevent further forcing of air into the pleural cavity. The tear should be given a chance to heal without interference. The air may be absorbed and the lung become expanded within 3 to 6 weeks. An intrapleural pressure which becomes increasingly negative calls for closing the pleural cavity. Intrapleural measurements therefore are of diagnostic aid.

In cases of recurrent spontaneous pneumothorax, attempts have been made to obliterate the pleural space by creation of an aseptic or sterile pleuritis by application of

irritants to the surface of the lung. The resulting inflammatory reaction causes thickening of the visceral pleura and prevents further rupture of the peripheral blebs. The materials used are the patient's own blood, 50 per cent glucose solution, 1 per cent nitrate of silver, gomenol in mineral oil or lipiodol or talc with or without sulfonamide. Good results have been obtained in numerous cases. Pleural leaks may be successfully closed (by suture of the involved area), emphysematous blebs excised, emphysematous cysts invaginated and ruptured bronchogenic cysts treated by excision or lobectomy. Recurrences following treatment have not been reported.

In cases of pneumothorax in which the pressure is positive and the patient is distressed by the high tension, clinical relief may be obtained by removal of the air through thoracic puncture by use of an indwelling wide-bored aspirating needle or a trocar and cannula inserted into the pleural cavity through the fifth intercostal space and attached to a water trap or constant suction apparatus. Aspiration of fluid may be required in cases of hydrothorax.

When the collapsed lung fails to re-expand because of fibrous adhesions, injections of streptokinase and streptodornase may be successful in producing hydrolysis of the fibrin. When the liquified material is repeatedly aspirated, the lung may re-expand, thereby eliminating the need for decortication.

*Prognosis*.—Prognosis is good in simple benign pneumothorax when the tear becomes sealed and the lung re-expands following absorption of the air. If a complication is present, such as tuberculosis, empyema, bronchiectasis or acute inflammation, the condition is serious. Tension pneumothorax impedes the circulation and is therefore dangerous. A chronic pneumothorax may develop if the air is not absorbed and the lungs fail to expand, but if fibrosis finally occurs the hole may be sealed and then the lung gradually expands. Development of a pyopneumothorax indicates the presence of an underlying tuberculosis or some other serious infectious process.

## Hydrothorax

Noninflammatory serous fluid may collect in one or both pleural cavities secondary to a constitutional disease, such as chronic heart disease or chronic nephritis, and cause a hydrothorax. Other causes may be cirrhosis of the liver, nutritional hypoproteinemia, lung or mediastinal tumor, Meigs syndrome, or pressure on the pulmonary veins. The fluid oozes slowly from the pleural tissues and accumulates. The pleural surfaces remain normal in appearance or slightly cloudy and swollen if the hydrothorax is long-standing.

The symptoms are those of pleural effusion and usually occur only when there is encroachment upon the heart and lungs. An associated edema of the lung will cause cough with expectoration. The transudates occur more often on the right than on the left side and, when bilateral, are more profuse on the right side. The roentgenologic findings are the same as those in serofibrinous pleurisy. A diagnostic thoracentesis will reveal the noninflammatory nature of the transudate, which is a clear, pale straw-colored fluid of low specific gravity (below 1.018), comparatively low cell count and a protein content of less than 5 per cent. It does *not* clot upon standing. The fluid may be aspirated but will recur unless the primary or initiating cause is removed.

## Hemothorax

*Etiology*.—Hemothorax is a collection of blood within the pleural cavity, resulting either from trauma or from an internal hemorrhage of an intercostal, mammary or pulmonary vessel. The trauma may result from a blow, from a stabbing, from a crushing of the chest, or from a gunshot wound. A fractured rib may lacerate the lung. Other occasional causes are pulmonary infarction, pneumococcal pneumonia, rupture of a thoracic aneurysm, blood dyscrasias, tuberculosis and invading carcinoma. A hemothorax accompanying a traumatic pneumothorax may simulate an acute abdominal disease and lead occasionally to unnecessary surgery. Life may be endangered if there is profuse bleeding or compression of

the lungs and great vessels or if infection occurs

*Clinical Features*.—Bleeding from the lung usually ceases in from 24 to 48 hours, when the intrapleural pressure becomes greater than that of the injured vessel. Time should therefore be given for the tear of the lung to seal spontaneously. Anti-shock therapy should be administered in the meantime, with supportive treatment. Secondary bleeding may take place soon after the first 24 hours because of compression of the lung and blood vessels, especially in the presence of a pneumothorax. *This should be prevented if possible.* If the first pleural effusion has not been evacuated before this occurs, the interpleural pressure may cause dangerous compression symptoms.

The physical signs of hemothorax, except for shock and collapse, are similar to those of hydrothorax. Progressive bleeding is evident from pallor, restlessness, thirst, increase in pulse rate and decrease in blood pressure. Displacement of the apex of the heart and dullness of the chest to percussion are important symptoms.

When the hemothorax becomes infected, symptoms of infection arise suddenly. *A diagnostic aspiration should be made and* antibiotic therapy administered.

*Treatment*.—Treatment consists in control of shock and hemorrhage by use of morphine, *blood and plasma transfusions and oxygen*. Unless these measures are successful in from 36 to 48 hours, measures must be taken to produce evacuation of the collected blood, *re-expansion of the lung and obliteration of* the cavity as rapidly as possible. If the bleeding is from an intercostal or mammary artery, ligation may be necessary. If from a hilar vessel or from deep laceration of the lung, suturing may be required, or in extreme cases lobectomy. If the hemothorax becomes purulent, underwater drainage should be used. Rib resection is often found necessary in cases of infected hemothorax.

Decortication of the organizing hemothorax has become an accepted procedure. In many cases, however, use of streptokinase (SK) and streptodornase (SD) may liquify the coagulum and permit its removal by aspiration. *Although it must be considered* as an adjunct to surgical management, in some cases it may make decortication unnecessary. Antibiotics are generally administered at the same time.

### Chylothorax

Chylothorax, a disease in which chyle is present in the pleural cavity, is usually caused by a traumatic rupture of the thoracic duct. Occasionally, it is a result of occlusion of the thoracic duct by lymphoblastoma or of various diseases, such as *pressure-producing inflammation of endo*-thoracic lymph nodes, perforating lymphadenitis, Hodgkin's disease, cirrhosis of the liver, filariasis, and ruptured aneurysm of the thoracic duct. On rare occasions chylothorax occurs subsequent to intrathoracic surgical injury of the thoracic duct. Although chylothorax is usually on the right side (except in cases due to penetrating injuries, which are more common on the left side), it may occur bilaterally.

The aspirated fluid is milky in appearance and has a fat content of from 0.4 to 4.0 per cent. The chyle is bacteriostatic and therefore resists putrefaction. It is rich in lymphocytes, *but the lymphocytes in the blood are* decreased.

*Clinical Manifestations*.—The disease is characterized by rapid onset with severe *symptoms which, however, are quickly* relieved by thoracentesis. In addition to the symptoms attendant upon any rapid pleural effusion, weight loss from malnutrition, *oliguria* and thirst occur. Without replacement of the lost fluid protein and fat, wasting and exhaustion may cause death within a few days or weeks. In some cases a partial equilibrium is established and though the patient does not regain his lost weight, further loss does not take place. The patient may then live in fairly good health for years. Many patients recover after simple aspiration of the fluid.

When suction drainage fails to bring about re-expansion of the lung and stoppage of chyle within from 10 to 14 days and the patient presents *a downhill course, surgical* ligation of the thoracic duct is indicated. Simple ligation should be sufficient to stop the loss of chyle permanently. Roentgen

therapy may be temporarily helpful in cases caused by lymphoblastoma of the mediastinum A high protein diet intravenous infusion of amino acids and an occasional blood transfusion are recommended

REFERENCES

*Diseases of the Pleura*


BALDERIDGE R R and LEWIS R L Traumatic Chylothorax Ann Surg *128* 1056 1948

FRIEDMAN I L and CARTER S B Empyema In KYSER F A Therapeutics in Internal Medicine New York Nelson 1950

LOWRY THOMAS Diseases of the Pleura In MYERS J A and MCKINLAY C A Chest and Heart Springfield Charles C Thomas V 1 1948

MEADE R H JR and BLADES B B Surgical Treatment of Recurrent and Spontaneous Pneumothorax of Nontuberous Origin Am Rev Tuberc 1949 *60* 683

MEADE R H *et al* Management of Chylothorax J Thoracic Surg 1950 *19* 709

MILLER J M *et al* Clinical Experience With Streptokinase and Streptodornase J A M A 1951 145 620

SHERRY S TILLETT W S and READ C T Use of Streptokinase-streptodornase in the Treatment of Hemothorax J Thoracic Surg 1950 20 393

SIBLEY J C Study of Two Hundred Cases of Tuberculous Pleurisy With Effusion Am Rev Tuberc 1950 62 314

TREVIS J W Empyema In CONN H F Current Therapy 1951 Philadelphia W B Saunders Co 7th ed 1947


## DISEASES OF THE MEDIASTINUM


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### MEDIASTINAL EMPHYSEMA

*Etiology* —Air may gain access to the mediastinum by a number of routes Chest injuries with wounds of the trachea major bronchi or esophagus may lead to massive mediastinal emphysema Infection foreign bodies and instrumentation which cause perforation of the same organs from within may produce mediastinal emphysema Surgery on the neck or cervical lacerations may permit air to dissect into the mediastinum and perforating injuries of the abdomen pneumoperitoneum and perirenal air insufflation have occasionally introduced air into the retroperitoneal space and thence into the mediastinum

In most cases no obvious etiologic factors are demonstrable Macklin has established the following chain of events in the usual cases increased intra-alveolar pressure rupture of an alveolus pulmonary interstitial emphysema entry of air into the mediastinum by dissecting along the perivascular sheaths of pulmonary vessels Invariably no basic lung pathology is demonstrable hence the term *spontaneous mediastinal emphysema* The condition may follow exertion as in childbirth but usually occurs while the victim is at rest

*Signs and Symptoms* —The complaints are usually a sudden onset of substernal pain radiating to the back or into the left shoulder and mimicking coronary thrombosis even to the point of radiating in rare instances down the arm to the fourth and fifth fingers of the left hand The pain is more often mild and unaccompanied by evidence of respiratory distress but with increasing *degrees of pressure within the mediastinum* the great veins collapse cardiac output is diminished and dyspnea and cyanosis appear The occurrence of such degrees of intramediastinal tension is commonly averted by the escape of air through intercommunicating fascial planes Inasmuch as the pretracheal and prevertebral fascia of the neck are continuous at their inferior margins with the anterior and posterior walls respectively of the mediastinum entry of air into the neck occurs with subsequent dissection through the subcutaneous planes of the body Pain in the chest has occasionally been observed to subside with the appearance of subcutaneous emphysema Another frequently associated finding is a spontaneous pneumothorax usually on the left resulting from a small rent in the mediastinal pleura This has raised the question of whether many spontaneous pneumothoraces may not be secondary to mediastinal emphysema

The *Hamman s sign of mediastinal* emphysema is a peculiar crunching or crackling sound synchronous with the heart beat This sound is due to compression by the *heart of the mediastinal air pockets overlying* the heart In fact the air over the heart

the lungs and great vessels, or if infection occurs

*Clinical Features.*—Bleeding from the lung usually ceases in from 24 to 48 hours when the intrapleural pressure becomes greater than that of the injured vessel. Time should therefore be given for the tear of the lung to seal spontaneously. Anti-shock therapy should be administered in the meantime, with supportive treatment. Secondary bleeding may take place soon after the first 24 hours because of compression of the lung and blood vessels, especially in the presence of a pneumothorax. This should be prevented if possible. If the first pleural effusion has not been evacuated before this occurs, the interpleural pressure may cause dangerous compression symptoms.

The physical signs of hemothorax, except for shock and collapse, are similar to those of hydrothorax. Progressive bleeding is evident from pallor, restlessness, thirst, increase in pulse rate and decrease in blood pressure. Displacement of the apex of the heart and dullness of the chest to percussion are important symptoms.

When the hemothorax becomes infected, symptoms of infection arise suddenly. A diagnostic aspiration should be made and antibiotic therapy administered.

*Treatment.*—Treatment consists in control of shock and hemorrhage by use of morphine, blood and plasma transfusions, and oxygen. Unless these measures are successful in from 36 to 48 hours, measures must be taken to produce evacuation of the collected blood, re-expansion of the lung, and obliteration of the cavity as rapidly as possible. If the bleeding is from an intercostal or mammary artery, ligation may be necessary. If from a hilar vessel or from deep laceration of the lung, suturing may be required or, in extreme cases, lobectomy. If the hemothorax becomes purulent, underwater drainage should be used. Rib resection is often found necessary in cases of infected hemothorax.

Decortication of the organizing hemothorax has become an accepted procedure. In many cases, however, use of streptokinase (SK) and streptodornase (SD) may liquefy the coagulum and permit its removal by aspiration. Although it must be considered as an adjunct to surgical management, in some cases it may make decortication unnecessary. Antibiotics are generally administered at the same time.

## CHYLOTHORAX

Chylothorax, a disease in which chyle is present in the pleural cavity, is usually caused by a traumatic rupture of the thoracic duct. Occasionally, it is a result of occlusion of the thoracic duct by lymphoblastoma or of various diseases such as pressure-producing inflammation of endothoracic lymph nodes, perforating lymphadenitis, Hodgkin's disease, cirrhosis of the liver, filariasis, and ruptured aneurysm of the thoracic duct. On rare occasions chylothorax occurs subsequent to intrathoracic surgical injury of the thoracic duct. Although chylothorax is usually on the right side (except in cases due to penetrating injuries, which are more common on the left side), it may occur bilaterally.

The aspirated fluid is milky in appearance and has a fat content of from 0.4 to 4.0 per cent. The chyle is bacteriostatic and therefore resists putrefaction. It is rich in lymphocytes, but the lymphocytes in the blood are decreased.

*Clinical Manifestations.*—The disease is characterized by rapid onset with severe symptoms which, however, are quickly relieved by thoracentesis. In addition to the symptoms attendant upon any rapid pleural effusion, weight loss from malnutrition, oliguria and thirst occur. Without replacement of the lost fluid protein and fat, wasting and exhaustion may cause death within a few days or weeks. In some cases a partial equilibrium is established and, though the patient does not regain his lost weight, further loss does not take place. The patient may then live in fairly good health for years. Many patients recover after simple aspiration of the fluid.

When suction drainage fails to bring about re-expansion of the lung and stoppage of chyle within from 10 to 14 days and the patient presents a downhill course, surgical ligation of the thoracic duct is indicated. Simple ligation should be sufficient to stop the loss of chyle permanently. Roentgen

ally shows a marked leucocytosis (15 000 to 30 000 leucocytes), with a significant shift to the left

*Treatment* —Massive amounts of antibiotics should be used Adequate dependent drainage is essential and is of particular value in the case of mediastinal abscesses This drainage may sometimes be effected through a cervical or paravertebral incision If the esophagus is perforated the patient must be kept in the Trendelenburg position with continuous suction at a point just above the perforation—and in the opinion of some with a gastrostomy below—to permit administration of food and fluids

*Chronic Mediastinitis* —*Definition* — Chronic mediastinitis is an uncommon disease in which the normal mediastinal areolar tissue is largely replaced by a dense network of fibrous connective tissue Distortion of the mediastinum results with pressure on the various enclosed structures

*Etiology* —Tuberculosis is by far the most common cause of this condition as the result of massive mediastinal node involvement Syphilis once contributed a significant number of cases of the same sort but this is no longer true By direct extension into the mediastinum actinomycosis blastomycosis and other pulmonary mycoses may produce extensive mediastinal fibrosis Finally chronic mediastinitis may in some instances represent the effects of an acute mediastinitis

*Signs and Symptoms* —As a result of the traction upon and compression of the trachea bronchi esophagus nerves and great veins a wide variety of symptoms may arise Substernal pain dyspnea chronic cough dysphagia hoarseness hiccough and superior vena-cava syndrome may appear

*Diagnosis* —The history and symptomatology are of considerable value in establishing a diagnosis of chronic mediastinitis Physical examination is not rewarding X rays reveal widening and increased density of the superior mediastinum plus numerous adhesions and extensive fibrosis involving the diaphragm the pericardium the pleural sac *etc*

*Treatment* —Therapy consists of treatment of the primary cause

BIBLIOGRAPHY

*Mediastinal Emphysema*

ADOCK J D Spontaneous Interstitial Emphysema of the Lung With Mediastinal Retroperitoneal and Subcutaneous Emphysema Arch Int Med 1943 *71* 650

HAMMAN L Mediastinal Emphysema J A M A, 1945 *128* 1

MACKLIN M T and MACKLIN C C Malignant Interstitial Emphysema of the Lungs and Mediastinum as Important Occult Complication in Many Respiratory Diseases and Other Conditions Medicine 1944 *23* 281

MILLER H Spontaneous Mediastinal Emphysema With Pneumothorax Simulating Organic Heart Disease Am J Med Sc 1945 *209* 211

*Acute Mediastinitis*

ADAMS R Acute Suppurative Mediastinitis J Thoracic Surg 1946 *15* 336

NEUHOF H and JEMERIN E E Acute Infections of the Mediastinum Baltimore Williams & Wilkins Co 1943

*Chronic Mediastinitis*

ERGANIAN J and WADE L J Chronic Fibrous Mediastinitis With Obstruction of the Superior Vena Cava J Thoracic Surg 1943 *12* 275

## DISEASES OF THE DIAPHRAGM

BY J WINTHROP PEABODY M D and J WINTHROP PEABODY JR M D

The diaphragm is the dome-shaped striated musculo-tendinous partition serving as the primary muscle of respiration and as a secondary muscle in venous return as well as separating the thoracic from the abdominal cavity

The embryologic derivation of the diaphragm is a fairly complex matter The anterolateral segment is derived from the septum transversum which in the early embryo originates in the cervical region (explaining the cervical innervation of this muscle via the phrenic nerves) The posterolateral portion of the diaphragm is derived from the pleuroperitoneal membrane and to some extent from the dorsal mesentery These structures eventually fuse but various malformations may result *e g* failure of the pleuroperitoneal membrane to develop (congenital absence of a part of the diaphragm) failure of the pleuroperitoneal membrane to fuse with the septum transversum (foramen of Bochdalek) weakness in

may obliterate the usual dullness obtained on percussion over the heart. Hamman's sign is pathagnomonic of mediastinal emphysema.

*Diagnosis.*—The most reliable diagnosis is clinical. X-ray examination may be confirmatory.

*Treatment.*—In severe cases a collar incision just above the manubrium through the deep cervical fascia may be lifesaving. Tracheotomy is never indicated, since vena-cava compression, rather than tracheal compression, is the source of the dyspnea and cyanosis. Milder cases require no particular therapy and may be followed on an ambulatory basis. The patient should be instructed to avoid coughing, straining at stool, *etc.*, so as not to increase the intra-alveolar pressure. A cough depressant may be indicated. Chemotherapy should be used only in the presence of active infection, not as a prophylactic measure.

## MEDIASTINITIS

*Acute Mediastinitis.—Definition and Etiology.*—Acute mediastinitis is never a primary disease but is always secondary either to primary infection elsewhere or to perforation of the esophagus or tracheobronchial tree. Esophageal injury is certainly the most common cause, it being responsible for about half of cases. It may result from such procedures as esophagoscopy, gastroscopy, and attempts at dilatation or from the ingestion of sharp foreign bodies, of which fish and chicken bones are by far the commonest. Less often, perforation results from esophagitis or carcinoma. Though the fragile wall of the esophagus predisposes to perforation, the sturdier structures of the trachea and bronchi reduce the possibility of rupture.

The next most common cause of acute mediastinitis is infection of the neck, which occurs predominantly in children. When mediastinitis is secondary to cervical or lung infection, the offending organism is chiefly a hemolytic streptococcus.

*Pathology.*—Since perforations fo the esophagus are more often at the pharyngoesophageal junction and most infections descend from the neck, the superior mediastinum is the more frequent location of acute mediastinitis. Both localized and diffuse forms of the disease occur; the localized form, the more common, is known as mediastinal abscess, the diffuse form is known as acute suppurative (phlegmonous) mediastinitis.

Acute suppurative mediastinitis may be accompanied by rapid extension of suppuration with little tendency toward localization or respect for anatomical boundaries. The entire mediastinum becomes bathed in pus. Although this kind of acute mediastinitis is more apt to follow cervical infection than esophageal perforation, it may nevertheless result from other causes. Penetration of the lung is not seen, but bilateral empyemas frequently occur from extension of the disease along peribronchial connective sheaths to the subpleural lymphatics.

*Signs and Symptoms.*—Sudden cervical or substernal pain upon swallowing a few hours after esophageal instrumentation or the ingestion of a foreign body is the classical picture of acute mediastinitis and is clearly elicited in a surprising number of instances.

All degrees of severity are encountered. Pain, the main symptom, is often intensified by swallowing and may indicate by its location the level of mediastinitis. There is usually a rather severe systemic toxicity. Such symptoms as brassy cough, hiccough, hoarseness, hyperpnea, and stridor may occur. The disease may be fulminating and rapidly fatal. If it is, prostration, high fever and evidence of venous compression (dyspnea and cyanosis) are found. Otherwise evidence of venous compression is unusual.

Physical examination is only of limited value. Anterior displacement of the trachea can sometimes be demonstrated (inability to insert the finger behind the suprasternal notch). Percussion may reveal a widened area of dullness overlying the mediastinum. Signs in the neck include tenderness, fullness, heat, and subcutaneous emphysema. There may be severe pain on moving the trachea. Occasionally evidence of mediastinal emphysema will be found.

*Diagnosis.*—In addition to the physical findings, a great deal may be learned from *x*-ray study. Examination of the blood usu-

ties constitute about 70 per cent of all diaphragmatic hernias.

(3) *Short Esophagus Type* (true thoracic stomach). — As the term implies, this type of diaphragmatic hernia is dependent upon a short esophagus, that is, an esophagus of insufficient length to permit the stomach to lie completely below the diaphragm. It may be congenital in origin or acquired by contraction secondary to chronic inflammation. Unlike the other types, this kind of hernia cannot reduce itself, for it is fixed, not sliding. The esophagus terminates at the very apex of the stomach. About 8 per cent of diaphragmatic hernias fall into this group.

*Signs and Symptoms.* — Many cases are asymptomatic. When present, clinical manifestations may vary with the size and reducibility of the hernia, but one cannot help being impressed by the frequency with which severe symptoms arise from a small hernia. In such instances the element of diaphragmatic muscle spasm around the hiatus is undoubtedly of great importance.

A vague sense of mild epigastric distress, variously described as a "fullness," "heartburn," "indigestion," or actual pain, is the usual chief complaint. The classic picture is the occurrence of such pain during or following a heavy meal, with aggravation upon lying down or stooping over, followed on some occasions by relief from belching, vomiting, or by merely walking about. The pain may be primarily nocturnal in occurrence and prevent the patient from sleeping in the recumbent position. Diaphragmatic spasm may produce referred pain in the left neck, shoulder, or down the arm. Couple such symptoms with substernal oppression, a rapid pulse and palpitation due to a slight displacement of the heart from the hernia, and it is easy to see how an erroneous diagnosis of angina pectoris can be made. Harrington found the most frequent errors in diagnosis to be gall bladder disease and peptic ulcer.

Regurgitation or gaseous eructation may be the sole complaint, but again characteristically follows meals and is apt to be precipitated by reclining or bending over, although satisfactory egress of gas and gastric contents may be impeded by concomitant spasm of the diaphragm. The patient may be aware of a gurgling sound within the chest on deep inspiration. Not infrequently the severe case leads to such an association of pain and vomiting with meals that the patient develops "food fear," limits himself to a very small dietary intake, and loses weight.

Esophagitis, gastritis, or ulceration may result from reflux of acid gastric contents, sliding motion of the hernia, or constriction from the diaphragmatic spasm. The associated dysphagia may be severe. Profuse hematemesis and melena are uncommon, but the persistent presence of occult blood in the stool will often produce a moderate secondary anemia.

With large hernias, respiratory or cardiac embarrassment may occur. If the colon is involved in the hernia, obstipation and evidence of intestinal obstruction may result.

*Diagnosis.* — Esophageal hiatus hernias may be suspected on routine chest films, but the definite diagnosis depends upon *x*-ray and fluoroscopic studies after ingestion of an opaque material. By coating the esophagus and stomach with a thin coat of barium several pertinent findings can be obtained.

X-ray is of assistance in ruling out other conditions, including *eventration of the diaphragm*. The latter is a rare condition of unknown etiology characterized by an atonic elevated hemidiaphragm which, on gross examination, proves to be thin, translucent, and similar to the diaphragm that has been paralyzed. It is characteristically asymptomatic but may be associated with vague gastrointestinal or respiratory symptoms. More often than not it is merely an incidental finding, giving the picture of a high curved leaf of the diaphragm, usually on the left, hence having the gas bubble of the stomach immediately below. The striking fluoroscopic finding is that found with any paralyzed diaphragm, namely, paradoxical ascent (rather than descent) of the involved hemidiaphragm on inspiration. This is caused by the relative increase in intra-abdominal pressure during inspiration, with the result that the relaxed diaphragm is pushed upward while the normal leaf contracts downward. Barium swallow will prove negative in cases of eventration, which may afford the only means of differentiating

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or enlargement of the foramen of Morgagni, and, finally defects in the esophageal hiatus One type of the latter may result from an esophagus which failed to grow to a sufficient length to permit the stomach to occupy *its normal position below the diaphragm* (thoracic stomach)

*Dysfunction of the Diaphragm* —This manifests itself in abnormal position of the diaphragm The position which it takes under normal as well as pathologic conditions depends in the first place upon its own tonus which overcomes both the positive intra abdominal and the negative intrathoracic pressures Since the tonus changes in the diaphragm depend upon the pressure differences between the thoracic and abdominal cavities this difference will have its influence upon the position of the diaphragm When it loses its tonus its position will come to depend altogether upon these differences in the pressure in the two cavities The *toneless diaphragm will be sucked up into* the chest with every inspiration and left to flop back in every expiration (paradoxical movements in diaphragmatic palsy) It may on the other hand be pushed down into the abdomen by increased intrathoracic pressure such as occurs in pulmonary emphysema pneumothorax or pleural effusions

*Elevation of the diaphragm* will thus be observed under the following circumstances (1) in the presence of increased abdominal pressure as in ascites or meteorism This is particularly the case if the abdominal pressure increases abruptly while slow *increase* of abdominal pressure such as occurs in pregnancy or abdominal tumors may be compensated for a long time by elevation of the lower ribs and increase of the diaphragmatic tonus (2) in the presence of increased thoracic pull such as is exerted by retractive processes in the lungs and pleura or pulmonary collapse (3) in the presence of reduced diaphragmatic tonus such as occurs in relaxation of the diaphragm whether congenital or acquired or in phrenic nerve palsy

The most frequent *form of elevation of* the diaphragm due to reduced tonus is that arising in paralysis of the phrenic nerve which is now so frequently produced artificially as a method of treatment in various pulmonary diseases, particularly tuberculosis

Descent of the diaphragm on the other hand, will be observed under the following circumstances (1) decreased thoracic suction as occurs in some cases of emphysema, of asthma, and in pleural effusion (2) decreased abdominal pressure such as is seen in general visceroptosis (3) increased diaphragmatic tonus associated with diaphragmatic spasm in such nervous disorders as hiccough encephalitis tetanus and in some cases of poliomyelitis

## ORGANIC DISEASES OF THE DIAPHRAGM

DIAPHRAGMATIC HERNIA —Herniation of abdominal viscera into the thorax may result either from defects in the normal diaphragmatic openings or from abnormal openings due to congenital malformation or trauma

*Esophageal Hiatus Hernia* —Herniation through the esophageal hiatus constitutes the major source of diaphragmatic hernias in adults Many are completely asymptomatic being picked up as incidental findings in *x* rays for other purposes Brick found an incidence of slightly over 300 hiatal hernias in one series of 3500 consecutive upper gastrointestinal series It was once thought to involve predominantly females preferably fat multiparous ones but this predilection appears exaggerated Several types occur

(1) *Paraesophageal Type* —Here the esophagus is of normal length with the lower end fixed below the diaphragm while a small portion of the gastric cardia herniates through the hiatus alongside the esophagus into the posterior mediastinum

(2) *True Hiatus Hernia* —With this type the esophagus is of normal length but not only the stomach is found to have ascended above the diaphragm but also the distal portion of the esophagus Moreover the amount of stomach above the neck of the hernia is usually larger than with the para esophageal type so that it has been proposed that the true hiatus hernia represents perhaps a more advanced stage of the paraesophageal hernia Together these two varie-

ties constitute about 70 per cent of all diaphragmatic hernias

(3) *Short Esophagus Type* (true thoracic stomach) — As the term implies this type of diaphragmatic hernia is dependent upon a short esophagus that is an esophagus of insufficient length to permit the stomach to be completely below the diaphragm It may be congenital in origin or acquired by contraction secondary to chronic inflammation Unlike the other types this kind of hernia cannot reduce itself for it is fixed not sliding The esophagus terminates at the very apex of the stomach About 5 per cent of diaphragmatic hernias fall into this group

*Signs and Symptoms* — Many cases are asymptomatic When present clinical manifestations may vary with the size and reduceability of the hernia but one cannot help being impressed by the frequency with which severe symptoms arise from a small hernia In such instances the element of diaphragmatic muscle spasm around the hiatus is undoubtedly of great importance

A vague sense of mild epigastric distress variously described as a fullness heart burn' indigestion or actual pain is the usual chief complaint The classic picture is the occurrence of such pain during or following a heavy meal with aggravation upon lying down or stooping over followed on some occasions by relief from belching vomiting or by merely walking about The pain may be primarily nocturnal in occurrence and prevent the patient from sleeping in the recumbent position Diaphragmatic spasm may produce referred pain in the left neck shoulder or down the arm Couple such symptoms with substernal oppression a rapid pulse and palpitation due to a slight displacement of the heart from the hernia and it is easy to see how an erroneous diagnosis of angina pectoris can be made Harrington found the most frequent errors in diagnosis to be gall bladder disease and peptic ulcer

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one condition from the other. Although eventration was once viewed with some alarm, we have now learned not to get excited over any degree of diaphragmatic rise and may in fact try to increase such a rise in patients with pulmonary cavitation by the induction and maintenance of an artificial pneumoperitoneum.

*Treatment.*—Medical management is possible in many mild cases and is advisable in elderly patients with minimal if any complaints. *A bland diet of nonbulky small* meals may afford relief. Antacids, antispasmodics and sedatives may obtain dramatic results and are of particular merit in the presence of esophagitis or ulceration. If strictures should be found, and it is especially important to rule them out by esophagoscopy, careful dilatation will often obtain a considerable amelioration of symptoms. When distressing complaints persist despite an ulcer regime and these other measures it is necessary to resort to surgery.

*Congenital Diaphragmatic Hernias.*—With the exception of diaphragmatic hernias following trauma and the small paraesophageal hernias following atrophy of the diaphragmatico-esophageal membrane practically all diaphragmatic hernias are dependent upon an element of congenital maldevelopment. Less definite in this regard are the esophageal hiatus hernias and those through the foramen of Morgagni, both of which tend to wait until middle age before *presenting themselves*. On this account these two types have, for descriptive purposes, been discussed previously. There remains a group in which the diaphragmatic *defects are larger and the symptoms much* earlier in onset so that the embryologic factor is quite striking. These have therefore been grouped under the heading of congenital hernias *and include primarily* those through the foramen of Bochdalek.

*Traumatic Diaphragmatic Hernias.*—Rents in the diaphragm may result from direct laceration as from a knife, *bullet or other* missile, or may result from indirect rupture due to crushing injuries of the chest or abdomen. Because of the liver barrier on the right most lesions occur on *the left*. Subphrenic abscesses are a rather common inflammatory source of diaphragmatic openings but do not lead to difficulty from herniation since they are on the right. A drainage tube in an empyema cavity has occasionally produced erosion *through the diaphragm*.

## ACUTE PRIMARY DIAPHRAGMITIS (HEDBLOM'S SYNDROME)

Acute primary diaphragmitis or Hedblom's syndrome is a primary myositis of the diaphragm seen after chilling or acute *infections of the upper respiratory tract*. It bears no relation to lesions of the diaphragmatic pleura, the lower lobes of the lung or the subphrenic organs, but lesions in these areas may follow as sequelae *of Hedblom's* syndrome. Clinically it is manifested by the presence of inspiratory pain in the lower chest, pain that cuts short the respiratory effort and prevents the patient from breathing beyond a certain depth. The respirations have a tendency to become costal in type and there is a limitation in the expansion of the lower portion of the chest wall. There is also a spasm of the abdominal muscles just below the costal margin with pain along the upper quadrants of the abdomen but no deep tenderness. The costal margin flares out and remains immobile. The patient generally complains of a re*ferred pain in the shoulder*, the trapezius ridge, and the supraclavicular area, pain caused by impulses through the phrenic and the related cervical nerves. Fluoroscopically *the diaphragm remains in a state of immobilization* in the midposition between inspiration and expiration. As the acute myositis subsides the muscle fibers may be replaced *by fibrous tissue and cause a flattening* out of the diaphragm, a flattening that has persisted for as long as thirteen years after the patient's recovery from the acute symptoms. *The inflammation may extend to the* diaphragmatic pleura and the subphrenic peritoneum, thus causing complications.

*Trichiniasis* is an important consideration *in the differential diagnosis because of the* primary diaphragmatic myositis due to involvement from the migrating trichinella larvae.

*Pleurodynia has often been confused* with Hedblom's syndrome. This condition is related to myositis of the intercostal muscles

and bears no relation to the diaphragm. It is characterized by constricting pain in the intercostal spaces and is aggravated by breathing. The same findings may also be found in *intercostal neuralgia* and *herpes zoster intercostalis*. Hedblom's syndrome is a self-limiting disease and clears up after one or two weeks. The treatment is symptomatic.

Secondary diaphragmitis may result from lesions in the lower lobe of the lung or in the subphrenic areas and cause symptoms similar to those of Hedblom's syndrome. In such cases the preexisting primary lesion is usually obvious.

BIBLIOGRAPHY

*Diaphragmatic Hernia*

BRICK, I. B.: Incidence of Hiatus Hernia and Associated Lesions Diagnosed by Roentgen Ray. Arch. Surg. 1949, *58*, 419.
DONOVAN, F. J.: Congenital Diaphragmatic Hernia. Ann. Surg., 1945, *122*, 569.
HARRINGTON, S. W.: Diaphragmatic Hernia. Monographs on Surgery. New York: Thomas Nelson & Sons, 1951.
HARRINGTON, S. W., and OLSEN, A. M.: Esophageal Hiatal Hernias of the Short Esophagus Type. Etiologic and Therapeutic Considerations. J. Thoracic Surg. 1948, *17*, 189.
MASTER, A. M., DACK, S., STONE, J., and GRISHMAN, A.: Differential Diagnosis of Hiatus Hernia and Coronary Artery Disease. Arch. Surg. 1949, *58*, 428.
SAHLER, O. D., and HAMPTON, A. O.: Bleeding in Hiatus Hernia. Am. J. Roentgenol. 1943, *49*, 433.

*Acute Primary Diaphragmitis*

JOANNIDES, M.: Acute Primary Diaphragmitis (Hedblom's Syndrome). Dis. Chest 1946, *12*, 89.

BRONCHIAL TUMORS

*Bronchiogenic Carcinoma.*—Once regarded as a lesion of rare occurrence, this neoplasm now rivals gastric carcinoma as the most common malignancy in man.

Two developments have undeniably tended toward the detection of a proportionately greater number of cancers of the lung: improved diagnostic facilities (x-ray, bronchoscopy, cytology) and better insight into the pathology of pulmonary neoplasms, many of which were formerly regarded as primary mediastinal tumors or tumors metastatic to the lung. Many, too, were obscured by overwhelming intercurrent infections that now respond to antibiotics.

*Incidence.*—Bronchiogenic carcinoma constitutes more than 10 per cent of all cancers found at autopsy. It is much more frequent in males than in females, the difference being at least 4:1 and in most recent series considerably higher. We must remember that the patient's age does not rule out the disease.

*Pathology.*—Histologically, bronchiogenic carcinomas are notorious for their extreme cellular pleomorphism. Nevertheless, it is possible in most instances to classify them according to the predominating cell type.

(1) *Epidermoid (squamous cell) carcinoma,* the most common type, consists of flattened epithelial cells arranged in concentric masses exhibiting varying degrees of keratinization with or without associated pearl formation. Although they are highly malignant, the epidermoid carcinomas tend to be slower growing than the other varieties and their local invasive propensities appear to overshadow their tendency toward distant metastasis. Because they most often involve large bronchi, the initial involvement is primarily hilar, with secondary invasion of the lung parenchyma and mediastinum.

(2) *Adenocarcinoma* (cylindrical-cell carcinoma) consists of cylindrical or columnar epithelial cells characteristically, though far from constantly, arranged in glandular patterns and sometimes showing evidence of mucin production (colloid type of adenocarcinoma). About 50 per cent of these tumors arise in the periphery of the lung. Early widespread metastases are common place. Probably the most striking clinical feature is the reversal of the sex incidence, women being involved equally as often as men and in some series even more often (Fried).

(3) *Undifferentiated* (anaplastic) carcinomas of the lung consist of a variety of cell types, namely, the round, the oat, and the spindle types. All have a scant cytoplasm and appear closely related one to the other. In each, the cells are usually closely packed and have a minimum of intervening stroma. This group shows the most rapid growth with a distinct predilection for early medias-

tinal invasions and wild lymphogenous and hematogenous dissemination

Insofar as the gross characteristics of these tumors are concerned there are no features that distinguish one type of bronchogenic cancer from another About 80 *per cent of* the tumors originate within the hilar portion of the bronchial tree and 20 per cent in the periphery The right lung is somewhat more often affected than the left

The spread of bronchiogenic carcinoma occurs in four known ways by direct ex-and inferiorly to the diaphragm, through which it may erode A rich network of lymphatics *interlaces the pulmonary paren* chyma to account for lymphogenous spread between lobes (this occurs often enough to *render simple lobectomy an inadequate* mode of therapy) By the time they are discovered about 75 per cent of the cases also show lymphatic extension to regional lymph nodes The bronchopulmonary nodes are first invaded then the tracheobronchial and paratracheal nodes (So frequently are



Fig 159 —Bronchiogenic carcinoma

tension by lymphogenous metastasis by hematogenous metastasis and by aerogenous spread Direct extension may take place in any direction *Because of the* predominantly hilar origin of bronchiogenic carcinoma the mediastinum is most often involved, and this entails encroachment on a variety of vital organs The more peripheral lesions may extend centrifugally to invade the pleura and thoracic wall superiorly to involve the brachial plexus, cervical sympathetics and other structures in the neck

the nodes involved that any attempt at curative surgery absolutely demands a thorough resection of them in addition to pneumonectomy *even though no spread* is apparent) Further lymphogenous dissemination follows the supradiaphragmatic abdominal retroperitoneal iliac, cervical, supraclavicular axillary and other lymphatic chains *The hematogenous route* is of the utmost importance and undoubtedly accounts for most of the metastasis to the contralateral *lung liver brain* skeletal

system adrenals and kidneys although lymphatic connections with the last two have definitely been demonstrated The aerogenous spreading of the exfoliated malignant cells is most unlikely

Massive metastasis may originate in a small primary lesion The most common sites of metastasis are the regional nodes (75 per cent) the liver and the contralateral lung (30 per cent) the bones the central nervous system, the adrenals and the kidneys (about 20 per cent) and the pericardium and the heart (15 per cent)

*Clinical Course* —The onset of bronchogenic cancer is usually insidious and has been frequently referred to as the silent phase because of the complete lack of symptoms Depending upon the size location and direction of growth a heterogenous group of symptoms soon appear Bronchial irritation leads to an irritative cough ulceration of the bronchial mucous membrane to hemoptysis Endobronchial growth results in partial obstruction of air flow manifested by varying degrees of wheezing and dyspnea If the mass should develop a ball-valve character, emphysema develops distal to the obstruction by permitting the entrance but preventing the exit of air Restricted drainage of normal secretions also occurs and leads to secondary suppurative disease peripherally Where obstruction becomes complete atelectasis of the occluded segment or lobe results

*Symptoms* —*Cough* is usually the first symptom to manifest itself and eventually accompanies practically every case Many individuals actually have a chronic almost lifelong cough and thus here a change in cough habit may be of great significance At first dry and irritative the cough later becomes productive as secretions pool behind the point of obstruction and in the event of infection becomes purulent and foul Eventually most patients show blood streaking It is to be stressed that until proved otherwise a persistent cough of unexplained origin occurring in a male patient of cancer age is prime evidence of bronchiogenic carcinoma In such an instance failure to obtain an *x* ray of the chest is inexcusable

*Hemoptysis* The sputum generally contains no more than streaks or flecks of blood When a copious quantity of blood occurs it is suggestive of adenocarcinoma Rienhoff has shown that hemoptysis and cough eventually occur in combination in 63 per cent of the cases

*Chest pain* is seldom an early complaint but ultimately occurs in 50 per cent of the cases and is one of the few things that will prompt the patient to obtain medical help Unlike pleurisy the pain is constant and unassociated with the respiratory cycle

*Weight loss* may be an impressive feature and accompanied by emaciation It may be out of all proportion to the size of the tumor or duration of the disease In fact it may be the initial sign but is usually relatively late

*Dyspnea* seldom occurs early but eventually appears in the majority of cases as the vital capacity is reduced by direct carcinomatous involvement of lung parenchyma and by such contributing factors as emphysema atelectasis infection pleural effusion and compression of the pulmonary artery and vein

*Unilateral wheezing* is an extremely valuable sign resulting from bronchial stenosis Not infrequently the wheezing is paroxysmal but can be brought out by forced expiration

In contrast to the aforementioned symptoms which are attributable to direct lung involvement there is a broad group of symptoms which result from metastasis When they occur in the absence of pulmonary symptoms they may present a most bizarre and puzzling picture

Mediastinal metastases may lead to involvement of the recurrent laryngeal nerve (hoarseness) especially on the left, where it traverses a longer course passing beneath the aortic arch involvement of the phrenic nerve (cervical pain and paralysis of the corresponding leaf of the diaphragm) compression or invasion of the esophagus (dysphagia) or invasion of the pericardium and heart (pericardial effusion or cardiac arrhythmias) Compression of the superior vena cava leads to the so-called superior-vena cava syndrome manifested by venous engorgement and cyanosis over the distribu

tion of the superior vena cava If acute, edema may be a prominent feature This syndrome usually occurs late and is of ominous significance

Extension through the superior thoracic strait may lead to a Pancoast syndrome, *consisting of ptosis of the upper eyelid* myosis, enophthalmus, anhidrosis and cutaneous flush (Horner's syndrome) due to cervical sympathetic nerve involvement along with pain and muscle atrophy in the shoulder girdle, arm, and hand due to brachial plexus invasion

Extension to the pleura may result in pleuritic pain or pleural effusion Such an effusion is classically sanguinous but need not be Malignant cells can generally be found in the sediment Not infrequently the pleura may be involved in sheetlike fashion similar to that described for pleural mesotheliomas (In fact, many of the reported mesotheliomas have been shown to be bronchiogenic cancers with an obscure primary site )

Diaphragmatic involvement particularly in the midportion may give rise to pain in the neck along the distribution of the phrenic nerve

Metastases to the central nervous system are predominantly cerebral and are quite common (about 20 per cent of cases) Similarly, of all metastatic malignancies in the brain those of pulmonary origin are by far the most common so much so that in *any case of an intracranial space occupying* lesion an *x* ray of the chest is mandatory

Metastases to bone occur in at least 20 per cent of the cases and probably in even more The vertebrae the ribs and the long bones appear to be affected in approximately that order of frequency Bone pain or a *pathologic fracture may accompany such* metastasis, but in other instances, the lesion may be completely silent and picked up only by a routine bone survey

Metastasis to the kidney may give rise to urinary symptoms such as hematuria Adrenal metastatic growths are usually small in size medullary in location and rarely give rise to signs of adrenal insufficiency

*Physical Signs* —Physical findings may be absent or scanty and are extremely variable depending upon the size and location of the tumor as well as on the degree of obstruction infection, effusion *etc* Almost any findings in the chest of a cancer age male must be closely checked for cancer, but physical findings alone are never diagnostic even in the presence of a unilateral wheeze *Pulmonary osteoarthropathy* is noted in 10 per cent of the cases and certainly should direct one to a study of the lungs It occasionally appears early but more often is a late sign

*Diagnosis* —The *sine qua non* of all early cancer detection is an awareness of its possible existence Nowhere does this aphorism find greater applicability than in the case of bronchiogenic carcinoma in which early symptoms appear trivial and are too often treated with indifference or at best with symptomatic therapy

1 *Roentgenography* although not without its shortcomings affords a *valuable diag*nostic implement

Body section radiography (tomography planography laminography) is of some value in confirming hilar lesions and should be utilized in any suspicious case Bronchography is rarely of value and may obscure future films

2 *Bronchoscopy* —It is now apparent that a positive bronchoscopy can be obtained in only about half of the cases Not only is it impossible to see most of the peripheral lesions by bronchoscopy but apical lesions even when seen are impossible to *biopsy Nevertheless the bronchoscope is* the best established means of obtaining a definite preoperative diagnosis Moreover, it may supply valuable information on the integrity of the vocal cords the proximity of the tumor to the trachea and the fixation of the trachea and evidence of carinal *involvement* (either directly or by an enlargement of a subcarinal node causing broadening of the angle of the carina) With the perfection of cytologic methods the aspiration of bronchial secretions from each lobe may give both a diagnosis and a location in an otherwise indiscernible case

3 *Cytology* is the newest diagnostic method and shows promise of becoming one of the best Specimens consist either of bronchial secretions obtained by bronchoscopy of sputum raised by deep cough Broncho-

scopic washings do serve more or less to localize a lesion but seem to exhibit no additional superiority whereas sputum has the advantage of being easily obtained This is of special significance for it has been shown that repeated studies of different specimens doubles the percentage of positive results Thus in only 35 per cent of all cases will one cytologic study confirm the diagnosis whereas 70 or 80 per cent of the cases will be confirmed by a series of five such examinations In cases of upper lobe lesions and lesions in the periphery cytology appears to have the greatest value for in these the bronchoscope *is practically worthless* *Epidermoid* and adenocarcinoma types are much more readily picked up than the undifferentiated carcinomas in which the cells are difficult to distinguish from inflammatory round cells Excessive enthusiasm should be discouraged but one must admit that the most encouraging prospect for the early diagnosis of bronchiogenic carcinoma lies in further advances along this line

4 *Aspiration Biopsy* —Although a fair percentage of positive results attend this method the hazard of carcinomatous seeding along the line of the needle puncture is sufficiently real to nullify whatever good results are obtained Other dangers such as hemoptysis infection and pneumothorax also exist Furthermore placing any confidence in a negative report might well lead in some cases to a disastrous delay in diagnosis

5 *Exploratory Thoracotomy* —In approximately 50 per cent of the cases no matter how exhaustive the workup a definite diagnosis cannot be established before operation Since operative surgery offers the sole means of diagnosing this group as well as the only chance of cure exploration in any given case appears justified on suggestive evidence alone so long as a comprehensive clinical investigation has been carried out

*Treatment* —*Pneumonectomy* with concomitant regional node dissection has been established as the treatment of choice *Lobectomy* is regarded as an inadequate procedure because it leaves behind adjoining lobes which may be simultaneously involved via the interconnecting lymphatics and because it hinders access to the mediastinal nodes which have been found to be involved at least microscopically in 75 per cent of the lungs resected The mortality rate from pneumonectomy for carcinoma runs about 15 per cent a relatively high figure but one that is continually decreasing and is actually somewhat lower in patients under 60 years of age Of all cases of bronchiogenic carcinoma probably about 15 per cent are resectable although various authorities publish a figure twice that Ochsner has demonstrated rather conclusively that the patients with palliative resections survive longer than those not considered for resection and *those who refuse resection* Moreover they are spared the element of sepsis and appear to die a less wretched death

The results of pneumonectomy depend almost entirely on the stage of the disease With localized malignancy the results are favorable Statistics show the survival rate following resection to drop precipitously for the first two years but to remain fairly level thereafter so that a patient who survives the second postoperative year stands a good chance of surviving 5 years Cases of epidermoid tumors stand the best chance for survival undifferentiated types the worst The conclusion is obvious that for eradication of the neoplasm diagnosis must be established early and surgical therapy applied quickly and vigorously

For patients considered inoperable *irradiation* may afford varying degrees of palliation Although the increased longevity is relatively brief in most instances it is enough to warrant irradiation in certain cases and a rare 5 year cure has been reported

*Nitrogen mustard* appears to offer symptomatic improvement in a relatively small percentage of cases but the improvement is transient and there is no significant prolongation of life Dramatic results with the drug have been described however in a number of cases of superior vena-cava syndrome

*Bronchial Adenoma* —Bronchial adenomas are uncommon tumors (about 5 per cent of all bronchial neoplasms) They may simulate bronchiogenic carcinoma although differing from the latter in several significant respects By contrast the bronchial aden

oma involves a younger age group, about half the reported cases having occurred in persons under 40, and affects the female more often than the male. Moreover, the adenoma typically runs a benign slow-growing course often marked by no more than a few symptoms. However despite the prolonged clinical course and amenability to bronchoscopic removal, one can no longer complacently refer to the lesion as benign. A few adenomas eventually undergo malignant degeneration to give rise to an undetermined but probably small percentage of bronchiogenic carcinomas. Of greater significance are the recent reports attesting to the occurrence of metastatic adenomatous involvement of mediastinal lymphnodes, liver, other organs and bone. In this light bronchial adenomas should more properly be considered carcinomas of low-grade malignancy.

Depending on the microscopic picture, two types of bronchial adenoma are described: the carcinoid adenoma (90 per cent of the cases) and the cylindroma or mixed type of tumor (10 per cent). The cylindromata are more apt to metastasize than the carcinoid adenomata.

The clinical picture is dependent on the degree of bronchial obstruction. The usual picture is that of a persistent aggravating cough which may be intensified on postural changes as on lying down and is more or less productive, this varying with the amount of secondary suppurative disease distal to the lesion. As one might anticipate from the richly vascular appearance of these tumors repeated episodes of hemoptysis usually occur and occasionally constitute the only symptom. A unilateral wheeze or recurrent bouts of respiratory infection are suggestive evidence in a young person. These tumors are slow growing but may eventually attain considerable size and then give rise to oppressive chest pain or dyspnea. Bronchiectasis or abscess formation may occur distal to the point of obstruction.

Bronchoscopic removal is possible when the lesion is pedunculated and free of extrabronchial extensions. Certainly, it is the only approach to adenomas involving the carina. In older persons, it may even be the procedure of choice but in general the age group in which adenomas are found renders the patients especially good candidates for resection. Resection also permits the obliteration of areas of secondary suppurative disease. Instances of local recurrence following bronchoscopic removal quite obviously demand lobectomy in all but extremely poor surgical risks.

*Hamartoma (Chondroma) of the Lung.*—Hamartomas are uncommon tumors occurring in various organs of the body. They consist of abnormal quantities and arrangements of the normal tissue structure of the organs they occupy. Thus chondromas of the lung are more appropriately referred to as hamartomas, containing as they do a preponderance of cartilaginous tissue in addition to other elements representative of normal bronchial wall. They are benign lesions but may mimic bronchiogenic carcinoma or echinococcic cyst. Surgical resection of the involved portion of the lung must be regarded as the only logical form of therapy.

*Hemangioma (Arteriovenous Fistula of the Lung).*—Hemangiomas of the lung are extremely rare tumors consisting predominantly of blood filled capillaries forming extensive intercommunications between the pulmonary artery and the pulmonary vein. A fair percentage are of the cavernous variety and serve as a pulmonary arteriovenous fistula.

*Clinical Course.*—The onset usually occurs in childhood. Males are affected more often than females. The characteristic picture is that of pulmonary osteoarthropathy, cyanosis and polycythemia in the presence of a pulmonary shadow of increased density on x-ray, but the shunt of blood may not be great enough to produce these signs. In about 50 per cent of the cases multiple telangiectasia and discrete hemangiomas of the skin and mucous membranes are present, often with a confirmatory history of epistaxis or gastrointestinal bleeding from a similar source in other members of the family. This relationship to Rendu-Osler-Weber disease is definite, the pulmonary hemangioma representing simply local evidence of a congenital tendency toward generalized malformation of the vascular system. Occasionally, auscultation over the location of the fistula will reveal a continuous bruit with accentua

tion in systole. The heart is normal but the electrocardiogram may show right axis deviation.

Angiocardiography seems to be the best diagnostic method and often shows rapid filling with delineation of the tumor.

Because of the many dangers attendant upon this lesion, surgical intervention is indicated in all but poor risk patients. Lobectomy is usually the method of choice.

*Alveolar Cell Carcinoma.*—(Pulmonary adenomatosis, malignant adenomatosis, diffuse primary alveolar carcinoma of the lung, carcinosis of the lung, terminal bronchiolar carcinoma.) Grossly, two types of pulmonary involvement have been described: a diffuse type wherein a picture resembling the stage of gray hepatization of lobar pneumonia may be found, with sticky surfaces similar to that of Friedländer's pneumonia; and a nodular type with multiple ill-defined nodular areas of consolidation somewhat like those seen with noncaseating miliary tuberculosis. No other primary tumor can be found elsewhere, thus ruling out the possibility of this representing metastatic involvement. In about 50 per cent of the cases the tumor is found localized in the lungs, usually without lymphatic extension; in the other 50 per cent, lymph node and/or visceral metastasis can be demonstrated.

The microscopic picture in alveolar-cell carcinoma consists of a striking hyperplasia of nonciliated mucus-secreting cuboidal or columnar epithelium lining otherwise unaltered alveolar walls. The most amazing feature is the presence of completely separate areas of obvious malignancy with preservation of intervening lung structure. Occasionally there is evidence of incipient hyperplasia in still another area.

Well worth noting is the close similarity of this entity to an epidemic virus disease of sheep called *jagziekte* or pulmonary adenomatosis. The histologic picture is identical but the cells are regular and metastases do not occur. Pulmonary adenomatosis of sheep is caused by a virus. While the latter has not been found pathogenic for man, the possibility of alveolar-cell carcinoma having some relationship to a virus is nevertheless an interesting consideration.

The clinical course of these patients is marked by a persistent cough which is dry initially but eventually becomes productive of copious quantities of a clear frothy sputum. This is fairly typical and depends upon increased output from the glandular cells of the alveoli. Dyspnea becomes prominent when a sufficient amount of functional alveolar lining is replaced by nonfunctional adenomatous tissue. Then extreme cyanosis occurs. Hemoptysis is notably absent in the majority of cases, as are fever and leucocytosis until the patient contracts a secondary infection. In the late stages cor pulmonale may occur, but pulmonary osteoarthropathy is seldom encountered.

The x-ray findings are in accord with the gross pathology. Attention should be devoted to the eosinophil count so as to rule out Loeffler's syndrome. Cytologic studies appear to be very rewarding.

No suitable form of therapy exists. Surgical intervention is of value in cases with unilateral involvement, and several 5-year cures have been reported following resection. The multicentric origin of these lesions, however, would appear to invalidate any claim for curative surgery. Irradiation and nitrogen mustard therapy have so far proved of no benefit.

### Mediastinal Tumors

*Teratoid Tumors (Teratomata and Dermoid Cysts).*—Teratoid tumors are uncommon tumors of embryonic origin. They probably arise as abnormal outgrowths of the third and fourth bronchial arches from which they separate to descend with the great vascular structures into the mediastinum. With the exception of lymphatic tumors, these are the most common neoplasms of the anterior mediastinum. They are most frequently of a cystic multilocu-lated type and may contain, in addition to undifferentiated cellular elements, vestigial structures such as hair, teeth, bone, *etc.* Solid teratoids are less often encountered but show a greater incidence of malignant changes. Some 70 per cent of all malignant teratoids arise from the solid variety.

In the majority of cases these tumors appear to lie dormant until puberty, when they

gradually begin to increase in size Radiologic evidence of the lesion can usually be demonstrated well in advance of the onset of symptoms Eventually the size and location of the tumor produce evidence of tracheal compression Resection is indicated on the basis of eventual malignant transformation of 12 per cent of cases

*Thymoma Thyroid Tumors Parathyroid Tumors* — See Chapter 16

*Neurogenic Tumors* — These constitute 90 per cent of all posterior mediastinal tumors and usually occur high in the paravertebral gutter

Other uncommon mediastinal tumors include *pericardial celomic cysts cystic hygromas bronchiogenic cysts gastroenterogenous cysts* and *tuberculomas* Rare instances of mediastinal *pheochromocytoma have been reported*

## Tumors of the Pleura

*Pleural mesothelioma* is a rare malignant tumor involving the pleura in a diffuse sheetlike manner and thereby surrounding and constricting although not invading the underlying lung Because some bronchiogenic carcinomas metastasize to the pleura in just such a fashion it has long been felt that reported cases of pleural mesothelioma probably originated in a small indiscernible primary site within the lung but enough well-documented cases have now been reported it seems to establish the authenticity of the true pleural mesothelioma

Grossly the pleura is markedly thickened and firm and grayish white in the areas of involvement which are usually fairly broad by time of discovery The visceral and parietal layers are both affected the pleural cavity being obliterated in some instances perfectly intact in others Pleural effusions are frequently encountered may be massive and are often bloody The lung exhibits varying degrees of atelectasis due to the constricting effect of the lesion but is usually not directly invaded By means of contiguous spread and serosal seeding the diaphragm peritoneum and pericardium often become studded with metastases Lymphatic metastasis to tracheobronchial mediastinal, retroperitoneal and cervical nodes are frequently encountered, and, in many instances the opposite pleura shows *involvement Occasionally* one encounters metastasis to the liver and other organs

Clinically, these tumors involve mainly the 40 to 60 year age group and occur about twice as often in males as in females The onset is insidious A nonproductive cough appears to be a common complaint Chest pain also frequently occurs early, is generally pleuritic and may be severe With loss of pleural elasticity, complete expansion is prohibited and dyspnea results This may be progressive and aggravated by pleural effusion Hilar adenopathy causes obstruction of bronchi with secondary suppurative disease emphysema, or atelectasis distally Expansion of the chest wall is usually greatly restricted on the involved side Progress is rapidly downward

X-ray examination may show evidence of pleural thickening This may be especially well brought out by producing a slight pneumothorax following thoracentesis Increased resistance to insertion of the needle in performing a thoracentesis is suggestive evidence, but even with extremely thick tumor this may be absent Cytologic study of the sediment from thoracenteses or a plug from the aspirating needle may establish the presence of malignancy yet only by exploratory thoracotomy can an absolute diagnosis be established

Treatment is largely symptomatic Repeated thoracenteses may be required for relief of dyspnea, but fluid almost invariably recurs with great rapidity All cases are fatal in from 6 to 9 months It is hoped that earlier recognition may permit extrapleural resection in some cases

## References

Ariel I M Avery E E Kanter J Head J J R and Langston H T Primary Carcinoma of the Lung Cancer 1950 *3* 229

Bubis S and Erwin J H Pulmonary Adenomatosis Am J Med 1949 7 336

Campbell, W N Pleural Mesothelioma Am J Path 1950 *26* 473

Clerf L H and Herbert P A The Value of Cytological Diagnosis of Pulmonary Malignancy Am Rev Tuberc 1950 *61* 60

De Bakey M E Ochsner A and Decamp P Carcinoma of the Lung Monographs on Surgery New York Thomas Nelson & Sons 1950

FRIED B M Bronchiogenic Carcinoma and Adenoma Baltimore Williams & Wilkins Co 1948
FRIEDMAN I L Tumors of the Pleura Dis Chest 1950 17 756
GRAHAM E A Considerations of Bronchiogenic Carcinoma Ann Surg 1950 13 176
GRAHAM E A and WOMACK N A The Problem of the So-called Bronchial Adenoma J Thoracic Surg 1945 14 106
MAIER H C Dermoid Cysts and Teratomas of the Mediastinum With Unusual Features Arch Surg 1948 5 154
McDONALD J R HARRINGTON S W and CLAGETT O T Hamartoma (Often Called Chondroma) of the Lung J Thoracic Surg 1945 14 128
MOERSCH H J TINNEY W S McDONALD J R and CLAGETT O T Symposium on Certain Tumors of Bronchi (Adenomas and Cylindromas) and on Tumors of the Trachea Proc Staff Meet Mayo Clinic 1946 21 410
OCHSNER A et al Primary Pulmonary Malignancy Factors Influencing Survival J Thoracic Surg 1948 17 573
OVERHOLT R H and SCHMIDT I C Silent Phase of Cancer of the Lung J A M A 1949 141 817
SEYBOLD W D McDONALD J R CLAGETT O T and HARRINGTON S W Mediastinal Tumors of Blood Vascular Origin J Thoracic Surg 1949 18 503
WEIR A B JR Pulmonary Adenomatosis Arch Int Med 1950 8 806

## CHEST INJURIES

By J WINTHROP PEABODY M D and J WINTHROP PEABODY JR M D

Injuries of the thoracic wall the lungs and the heart if not soon fatal remain of concern however slight they may seem because of the complications that may develop Injuries of the chest are of two types—penetrating and nonpenetrating—both equally serious Even without outward evidence of injury the ribs may be broken and lacerate the lung the diaphragm may be ruptured allowing the abdominal organs or blood from an injured liver to enter the pleural cavity or the injured thoracic wall may have torn the blood vessels and caused a hemothorax Blast injury results from sudden increased intrathoracic pressure caused by detonation of explosives

Injury to the thoracic wall or the lung produces a painful cough which the patient may try to repress with the result that the respiratory passages cannot free themselves from blood or other secretions and atelectasis may develop

*Clinical Features* —Patients with thoracic injuries should be hospitalized at once because of possible concealed injuries or complications The patient on examination is apprehensive and has a dry irritating cough perhaps with bloody sputum and the sides of his chest move unequally The alterations in the blood pressure respiration and pulse rates are indicative of shock If there is a gaping hole in the chest a sucking sound as of air being drawn inward can be heard and there may be a gurgling sound The thorax may be distended with air the mediastinum displaced toward the uninjured side A normal vesicular murmur on auscultation indicates air is entering the lung and increased intrapleural pressure is indicated by displacement of the apex beat and trachea A pleural or pericardial friction rub may later be heard A developing emphysema will produce a resonant sound on percussion or crackling sounds on auscultation Paradoxical breathing denotes a stove in chest and demands immediate surgical attention

Roentgenologic examination should be delayed until after emergency treatment if the patient s condition is serious unless perforation of the bowel is suspected The underlying viscera may be injured with or without fracture of the ribs Fracture of the ribs will be indicated by pain at the site of fracture limited expansion of the chest on the affected side difficult breathing and palpable bone crepitus

*Treatment* —Treatment is of three general types immediate therapy to prevent death careful watching for and treatment of complications and surgical repair of structural defects Immediate therapy includes control of hemorrhage treatment of shock and bringing the cardiorespiratory mechanism back to normal as soon as possible Blood transfusion and oxygen therapy should be administered at once in cases of severe injuries of the chest Antibiotics should be given freely parenterally or orally in all cases of obviously or potentially infected injuries

REFERENCES

KINSELLA T J Thoracic Injuries *In* Meyers J A and McKinlay C A Chest and Heart Springfield Charles C Thomas vol *1* 1948

SKINNER E F *et al* Chest Injuries in Civilian Practice Dis Chest 1950 *18* 363-75

## INHALATIONAL THERAPY

By ALVAN L BARACH M D

Although the physiological aspects of disturbances in respiration and circulation have been extensively studied, the practical application of these findings by appropriate physiologically directed treatment is more limited than our present knowledge would generally permit In fact relatively scant consideration has been accorded to the therapeutic use of gases and allied procedures in current text books on diseases of the lung and the heart despite increased admission that no emergency is more critical in clinical medicine than an interruption in the life-line of oxygen to the tissues

Respiration includes a two fold function

(1) External respiration concerned with the transmission of oxygen from the air to the arterial blood and the elimination of carbon dioxide from venous blood to the outer atmosphere the lungs and the respiratory passageway are primarily involved in this process

(2) Internal respiration concerned with the exchange of oxygen and carbon dioxide between the tissues and the blood the circulation the red corpuscles and hemoglobin and various enzymes concerned with oxidation are important links in internal respiration

The purpose of inhalational therapy may be described as an attempt to maintain or restore normal function in clinical disorders of external respiration Methods of treatment which developed from an understanding of the pathophysiology of these clinical entities are used to counteract functional or reversible pathology in the lungs and bronchi Although impairment of respiratory function ultimately manifests itself in a state of tissue oxygen want which may, at times be effectively treated by simple inhalation of an oxygen-enriched atmosphere, the recognition of more complex functional alterations in the respiratory system has stimulated the use of other gases as well as various types of pressure used either in conjunction with a therapeutic gas or with atmospheric air

### THE THERAPEUTIC USE OF OXYGEN

*Physiologic Aspects* —The central nervous system is most sensitive to damage by anoxia In recent years, the gradient of reaction in different parts of the brain has received special study The pathologic changes produced by anoxia may be initiated by various experimental methods, such as inhalation of low-oxygen mixtures carbon monoxide poisoning, and exposure to low barometric pressures In each instance a selective vulnerability of the brain has been described in the following order (1) the smaller pyramidal cells of the cortex (2) the Purkinje cells (3) the medulla retina and spinal cord and (4) the spinal root ganglions In these studies, the frontal lobe cortex was found to show pathological changes at times when the rest of the brain cortex was normal suggesting that the more recently developed elements in the central nervous system are more sensitive to injury perhaps because they require a higher oxygen consumption Cerebral anoxia has also been induced by increasing the oxygen up-take of the brain beyond the capacity of the existing oxygen supply as well as by decreasing the oxygen supply below the existing demand These and other findings in organic pathology of the brain as a result of anoxia have been correlated with functional disturbances created by inhaling low-oxygen atmospheres or by exposure to high altitudes Among the earliest symptoms of oxygen deficiency, produced by breathing 13 to 15 per cent oxygen or air at an altitude of 12,000 to 14,000 feet is impairment in emotional control, reason judgment and vision Other organs which are especially sensitive to anoxia include the heart the adrenal glands the kidneys and the lungs themselves

The degree of oxygen deficiency which takes place in clinical illness may be determined in certain instances by measuring the tension or saturation of the arterial blood

with oxygen The amount of oxygen which can be taken up by the hemoglobin and the plasma is primarily dependent upon the partial pressure of oxygen to which the blood is exposed The partial pressure of oxygen in the atmosphere is calculated by multiplying the percentage of oxygen by the barometric pressure after the pressure of water vapor has been subtracted At sea level 760 mm (the barometric pressure) minus 47 mm (pressure of water vapor) multiplied by 20 9 per cent, equals 150 mm or the partial pressure of oxygen in the atmosphere When either the barometric pressure or the concentration of oxygen is reduced the partial pressure of oxygen is lowered as follows

1 Reduced barometric pressure (360—47) × 20 9% = 65 4 mm
2 Reduced oxygen percentage (760—47) × 10% = 71 3 mm

In the first case, the partial pressure of oxygen in the atmosphere and in the alveolar air is lowered as a result of exposure to high altitude In the second instance of anoxia the partial pressure of oxygen in the arterial blood and in the alveolar air is decreased because of pathological changes either in the alveolar membrane and pulmonary capillaries as in pneumonia or congestive heart failure through accumulation of serous exudate in the alveoli as in edema of the lungs or because of inadequate and irregular ventilation of the air spaces as in pulmonary emphysema In the last case a lowered tension of oxygen in certain alveoli contributes unrespired blood to the aorta A decreased volume of breathing which occurs in respiratory paralysis due to poliomyelitis and excessive doses of sedative drugs likewise is followed by a lowered alveolar and arterial oxygen pressure

Under circumstances above mentioned a variable amount of reduced hemoglobin travels through the lungs without being adequately oxygenated which results in the characteristic bluish color known clinically as cyanosis However in patients who are anemic a low hemoglobin content may prevent the appearance of cyanosis even in the presence of severe arterial anoxia Furthermore the capillaries of the skin may be contracted as in shock in which case the bluish color may not be visible even in the presence of severe tissue oxygen want The concentration of carbon dioxide in the capillaries is also a factor which determines the presence or absence of visible cyanosis In conditions in which hyperventilation takes place a decrease in peripheral circulation is associated with an undue elimination of carbon dioxide

*Clinical Considerations* —Cyanosis is no longer relied upon as an indication of a deficient supply of oxygen to the tissues since it is generally a late sign Clinical judgment is necessary to appraise the degree of anoxia present especially such manifestations of impaired respiratory function as increased pulse rate irrationality dyspnea depressed breathing a grayish color to the face restlessness or irritability

In cardiac insufficiency the arterial blood may reveal only a slight decrease in saturation with oxygen, depending upon the degree of pulmonary congestion at a time when severe tissue oxygen lack is present The measurement of the oxygen saturation of mixed venous blood would be required in order to determine the degree of anoxia due to retarded circulation a procedure carried our in the Fick measurement of cardiac output in patients who receive special study Anoxia is a result of anemia may be diagnosed from analysis of the mixed venous blood, or estimated by the hemoglobin content

Serious local tissue anoxia may take place as a result of thrombosis of the coronary cerebral or other arteries without significant alteration of the arterial or mixed venous oxygen tension Nevertheless the administration of oxygen may be of crucial importance in these conditions because of the increase in the partial pressure of oxygen in the plasma of the collateral or partially occluded blood vessels even though no precise measurement of tissue anoxia can be obtained under these circumstances

Oxygen want produced by exposure to poisons which interfere with the oxidation mechanism in the cell is another kind of anoxia difficult to estimate In this class are included such histotoxic agents as cyanide and alcohol Cyanide produces its effect by inactivating the iron-containing oxygen car

REFERENCES

KINSELLA T J Thoracic Injuries *In* Meyers J A and McKinlay C A Chest and Heart Springfield Charles C Thomas vol 1 1948

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(1) External respiration concerned with the transmission of oxygen from the air to the arterial blood and the elimination of carbon dioxide from venous blood to the outer atmosphere the lungs and the respiratory passageway are primarily involved in this process

(2) Internal respiration concerned with the exchange of oxygen and carbon dioxide between the tissues and the blood the circulation the red corpuscles and hemoglobin, and various enzymes concerned with oxidation are important links in internal respiration

The purpose of inhalational therapy may be described as an attempt to maintain or restore normal function in clinical disorders of external respiration Methods of treatment which developed from an understanding of the pathophysiology of these clinical entities are used to counteract functional or reversible pathology in the lungs and bronchi Although impairment of respiratory function ultimately manifests itself in a state of tissue oxygen want which may at times be effectively treated by simple inhalation of an oxygen-enriched atmosphere the recognition of more complex functional alterations in the respiratory system has stimulated the use of other gases as well as various types of pressure, used either in conjunction with a therapeutic gas or with atmospheric air

### THE THERAPEUTIC USE OF OXYGEN

*Physiologic Aspects* —The central nervous system is most sensitive to damage by anoxia In recent years the gradient of reaction in different parts of the brain has received special study The pathologic changes produced by anoxia may be initiated by various experimental methods such as inhalation of low-oxygen mixtures carbon monoxide poisoning and exposure to low barometric pressures In each instance a selective vulnerability of the brain has been described in the following order (1) the smaller pyramidal cells of the cortex (2) the Purkinje cells (3) the medulla, retina and spinal cord, and (4) the spinal root ganglions In these studies, the frontal lobe cortex was found to show pathological changes at times when the rest of the brain cortex was normal, suggesting that the more recently developed elements in the central nervous system are more sensitive to injury, perhaps because they require a higher oxygen consumption Cerebral anoxia has also been induced by increasing the oxygen up-take of the brain beyond the capacity of the existing oxygen supply as well as by decreasing the oxygen supply below the existing demand These and other findings in organic pathology of the brain as a result of anoxia have been correlated with functional disturbances created by inhaling low-oxygen atmospheres or by exposure to high altitudes Among the earliest symptoms of oxygen deficiency, produced by breathing 13 to 15 per cent oxygen or air at an altitude of 12 000 to 14 000 feet is impairment in emotional control reason judgment and vision Other organs which are especially sensitive to anoxia include the heart the adrenal glands, the kidneys, and the lungs themselves

The degree of oxygen deficiency which takes place in clinical illness may be determined in certain instances by measuring the tension or saturation of the arterial blood

precipitated by respiratory infection the opportunity of a gradual program of oxygen administration is not available However an understanding of the possibility of respiratory acidosis should be kept in mind and oxygen administered in as low concentrations as are consistent with the safety of the patient in respect to the menace of anoxia The treatment for respiratory acidosis is difficult Intravenous sodium lactate has been employed by the author with evidence of clinical improvement Increasing the ventilation of the patient by a mechanical resuscitating device will also be of help

In patients with congestive heart failure either due to acute or chronic cardiac insufficiency relief of dyspnea is not accompanied by respiratory acidosis of any significant degree The pulmonary ventilation is lowered but the rise in $CO_2$ tension is apt to take place in a more gradual manner allowing the compensatory mechanisms to come into play before respiratory acidosis of significant degree manifests itself Carbon dioxide diffuses into the expired air more readily in passive pulmonary congestion than in either organic or functional pulmonary emphysema due to severe asthma in which many alveoli are poorly ventilated

The use of oxygen in patients with depressed respiration such as respiratory paralysis occurring in poliomyelitis should be controlled if possible by a determination of the arterial or alveolar $CO_2$ tension and the pH of either arterial or venous blood Although oxygen is frequently indicated in respiratory paralysis the degree to which the ventilation may be decreased is not easily measured Some form of mechanical breathing such as the tank respirator is indicated under circumstances in which oxygen relieves anoxia but not elimination of carbon dioxide Similarly in conditions in which the respiration may be depressed by drugs oxygen is best given in conjunction with devices which maintain an adequate pulmonary ventilation

In patients with obstructive dyspnea such as bronchial asthma with an associated functional over inflation of the lungs increase in carbon dioxide content with respiratory acidosis may occasionally take place and deserves appropriate treatment as outlined above In most instances however the proprioceptive reflexes in patients with asthma are sufficiently stimulated to maintain an adequate volume of ventilation which prevents respiratory acidosis unless excessive doses of barbiturate drugs have been employed In the treatment of local ischemic anoxia respiratory acidosis is not a factor Relatively high concentrations of oxygen from 60 to 70 per cent are frequently indicated continuously in such acute anoxic states as coronary thrombosis and cerebral thrombosis

Although oxygen in high concentrations may be given by mask for short periods of time the discomfort generally produced by continuous application of a mask renders it a less suitable agent than either the nasal catheter or the oxygen tent The maintenance of a concentration of 50 to 60 per cent oxygen by a flow of 12 liters to 15 liters per minute is now generally possible with the mechanically air-conditioned tent Undue accumulation of carbon dioxide will necessarily take place in any tent in which a flow of oxygen of less than 10 liters a minute is administered Even low concentrations of carbon dioxide in a tent tend to provoke increasing dyspnea in patients with pulmonary and cardiac disease The Meter mask has the advantage of not permitting re breathing and is generally to be preferred to the BLB apparatus in which concentrations of carbon dioxide of 2 per cent are frequently present during the administration of moderate flows of oxygen such as 4 to 5 liters per minute Furthermore the resistance in the sponge rubber discs of the BLB mask results in increased inspiratory effort when the valves function by admitting air from the outside atmosphere The fact that a prescribed concentration of oxygen from 40 to 100 per cent can be accurately administered with the injector of the Meter mask is an additional reason for employing this apparatus in routine oxygen therapy A description of the proper methods of carrying out the various procedures of inhalational therapy is beyond the province of this chapter they have recently been emphasized in the publication of the Standards of Effective Administration of Inhalational Therapy by the Committee on Public Health Rela

rier of the tissue cell which is a hematin compound cytochrome distinct from hemoglobin but related to it and capable of combining reversibly with oxygen Alcohol produces its effect by stabilizing oxycytochrome so that oxygen is not removed from the cell at the normal rate Inhalation of high oxygen atmospheres may increase the proportion of total cytochrome in the oxygenated form and thereby counteract to some extent the diminution of catalytic efficiency which the cytochrome suffers in contact with alcohol

A program of oxygen treatment depends upon an estimation of the degree of either arterial stagnant or other anoxia present as well as the calculated response to oxygen therapy based on previous experience in the clinical entity being treated In the use of oxygen for the prevention or treatment of anoxia in lobar or broncho pneumonia, the inhalation of a 50 per cent oxygen-enriched atmosphere is usually employed, since restoration of the arterial saturation to or near the normal value is generally obtained by this increase in alveolar oxygen In more severe anoxia the oxygen concentration is increased to 60 or 70 per cent but the administration of 100 per cent oxygen is allowed for no longer than 12 hours since irritant effects are produced in the lungs by concentrations of 80 per cent or above when inhaled continuously for prolonged periods

Relief of anoxia in pneumonia is generally accompanied by disappearance of cyanosis if present, a slight or moderate decrease in respiratory rate or volume diminution of dyspnea and restlessness The carbon dioxide content of the arterial blood is not significantly altered unless widespread bilateral disease is present The patient is treated with continuous administration of oxygen until the pneumonic process in the lungs has cleared sufficiently to allow removal from the oxygen-enriched atmosphere without an increase in pulse rate of over 10 or 15 beats per minute and without recurrence of dyspnea In extensive involvement of both lungs, abrupt removal from an oxygen-enriched atmosphere may provoke sharp return of obvious impairment of respiratory function

When the clinical entity being treated with administration of 50 per cent oxygen belongs to the group of cases in which a marked decrease in pulmonary ventilation takes place a respiratory acidosis may ensue because of inadequate elimination of carbon dioxide The onset of this complication is especially apt to take place in patients with pulmonary emphysema who are given high concentrations of oxygen to relieve chronic anoxic dyspnea, or who are treated for acute anoxia because of an exacerbation of dyspnea due to intercurrent respiratory infection The decrease of the volume of breathing engineered by the effect of oxygen on the carotid sinus is followed by relief of dyspnea without, however, a prompt development of the compensatory elimination of chlorides and retention of base and an adequate mechanism for excreting carbon dioxide in a decreased volume of breathing Under these circumstances, an increase in arterial $CO_2$ tension takes place with a rapid shift in pH toward acidity Delirium and coma may result with other manifestations of acidosis Because of the presence of irregular ventilation of alveolar cells which in many cases are deficiently diffused with air even prior to oxygen administration accumulation of $CO_2$ takes place with great rapidity even though dyspnea has been relieved through inhalation of high concentrations of oxygen

In cases in which oxygen administration is contemplated for these patients with chronic anoxic dyspnea acidosis may be avoided by a program of gradually increasing the concentration of oxygen delivered to the patient such as the use of the nasal catheter with a flow of one liter of oxygen per minute on the first day of administration increasing the flow every two to three days by one liter a minute until the desired rate 6 or 7 liters per minute is obtained At this time the treatment may be continued in a tent with 50 per cent oxygen without respiratory acidosis or mental changes of an adverse nature taking place even though the $CO_2$ content and tension of arterial blood have become elevated markedly above normal Compensation to the increased $CO_2$ tension in the blood is gradually developed by retention of base and elimination of chlorides from the urine In cases in which acute anoxia has been

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tions of the New York Academy of Medicine, and are given in detail in the author's textbook

When oxygen is administered for the purpose of restoring compensation in chronic pulmonary or cardiac disease, the termination of treatment is carried out by gradual decrease in the concentration of oxygen in the atmosphere The decrease in hemoglobin and red blood cell count that takes place as a result of oxygen treatment over long periods of time is one of the mechanisms which should be counteracted in reverse by a gradual exposure of the patient to an oxygen atmosphere that approaches that of air

### The Therapeutic Use of Carbon Dioxide

When it became apparent that carbon dioxide regulated respiration in a precise way the ventilation increasing with the increased concentration of $CO_2$ in the alveolar air the use of carbon dioxide as a therapeutic agent was developed primarily in order to produce an augmentation of breathing At one time it was thought that carbon dioxide was lost from the blood at times as a result of dyspnea in a variety of clinical entities with the result that a condition of alkalosis took place but this reaction now appears to be rare indeed When respiratory alkalosis does take place, engendered by hyperventilation the hemoglobin is bound more tightly to oxygen and the tissues are exposed to a low oxygen tension even though the hemoglobin itself may have an increased oxygen concentration When an unduly increased volume of breathing occurs as a response to anoxia as at high altitude, the remedy for the situation is plainly that of providing an increased oxygen atmosphere and not carbon dioxide

In clinical illness, the use of carbon dioxide has been largely abandoned since the evidence on which its employment was based has not been supported by more careful studies which have revealed respiratory acidosis with elevated arterial carbon dioxide tension in conditions such as sedative and narcotic poisoning atelectasis of the lungs of the newborn and other kinds of respiratory failure Even in the treatment of carbon monoxide poisoning in which the inhalation of 5 to 7 per cent $CO_2$ with oxygen displaces CO from hemoglobin the superiority of carbon dioxide in oxygen over inhalation of pure oxygen alone has been seriously questioned

In any form of obstructive dyspnea a carbon *dioxide concentration* above 1 per cent or more results not only in increased ventilation but in an increase in the negative pressure within the chest necessary to pull air into the lungs with the result that an increased tendency for exudation of serum and mucus in the respiratory passageway takes place When an increase in the volume of breathing is required the use of oxygen enriched atmospheres combined with some form of mechanical ventilation is generally indicated rather than carbon dioxide, which would increase the respiratory acidosis generally present In postoperative conditions deep breathing is no longer carried out by inhalation of high $CO_2$ concentrations as in some instances carbon dioxide acidosis is already present Turning the patient on the side or ventilating the patient after operation by intermittent pressure on the anesthesia bag is preferable

The use of 5 to 10 or, at times 15 per cent carbon dioxide in the treatment of intractable hiccup constitutes its main value at the present time When carbon dioxide is administered until the patient almost loses consciousness 2 to 3 minutes for 10 per cent $CO_2$ and 1½ minutes for 15 per cent $CO_2$ the hiccup may be relieved The procedure is often repeated at 3 hour intervals with marked clinical benefit The inhalation of high concentrations of carbon dioxide between 15 and 30 per cent has been used in the treatment of psychosis Dyspnea disorientation and a rise in systolic blood pressure takes place before onset of unconsciousness which is the goal of treatment in clinical entities such as dementia praecox and certain psycho-neuroses

### The Therapeutic Use of Helium

Helium was introduced as a therapeutic gas in 1934 for the treatment of intractable bronchial asthma and obstructive dyspnea

due to constricted lesions in the respiratory passageway. When helium is substituted for nitrogen a uniform mixture of the two gases takes place which then has the property of a single gas one third lighter than air.

The lighter the gas the more rapidly it diffuses, the formula being: the rate of diffusion of a gas is inversely proportional to the density of the gas (Graham's law). When a mixture of 80 per cent helium and 20 per cent oxygen is in the alveoli the increased rate of diffusion in comparison to air is as 1.7 to 1. The physical advantage of more rapid diffusion of a helium-oxygen mixture is observed in atelectasis of the lungs, obstruction of the Eustachian tube produced either by rapid descent in an airplane or too swift ascent to air at atmospheric pressure after previous exposure to increased pressures in tunnels. Similarly the passage of a gas through a constricted orifice varies inversely with the square root of the molecular weight of the gas or gas mixture. Thus a regulator attached to an oxygen cylinder at a flow of 1 liter per minute will deliver a velocity flow of 1.7 liters when attached to an 80 per cent helium—20 per cent oxygen cylinder.

In studies carried out by subjecting a spirometer to mechanical movement and having it breathe various gases through fixed orifices, either the velocity of movement of the helium-oxygen mixture could be increased at a constant pressure or the pressure lowered to effect a constant velocity of gas movement. The advantage of inhaling the helium-oxygen mixture is increased in proportion to the extent to which the constriction is localized, which results in turbulence, and decreased if the narrowing is prolonged in a linear direction, since the viscosity of helium is greater than that of nitrogen.

In obstructive dyspnea the effect of the helium-oxygen mixture makes possible a shorter period of inspiration with the consequence that a more normal volume flow of respiration is achieved with less effort. This finding has been confirmed by measuring the decrease in intrapleural negative pressure during inspiration in a patient with severe bronchial asthma and in experimental tracheal obstruction in dogs.



In bronchial asthma intermittent inhalations of an 80 per cent helium—20 per cent oxygen mixture are given to relieve severe dyspnea and in addition to provide a cumulative effect of bronchial relaxation which is produced by the physical influence of decreased respiratory effort. In constricting lesions of the respiratory passageway helium-oxygen mixtures have been given continuously at times with the result that tracheotomy for laryngeal dyspnea has been averted. Better alveolar ventilation as a result of inhalation of helium-oxygen mixtures has been responsible for its use in unresolved pneumonia, atelectasis of the lungs in adults and in the newborn infant.

The most feasible method of administration is the use of the Meter mask with an expiratory pressure of 2 to 3 cm. of water. The strict avoidance of rebreathing masks in the treatment of any type of bronchial obstruction is necessary since there already is increased carbon dioxide retention in this condition. The increased expiratory pressure maintains a wider lumen of the smaller bronchi during expiration and facilitates elimination of the inspired atmosphere with the use of increased contraction of the abdominal and lower intercostal muscles. The relief of obstructive dyspnea is enhanced when pressure breathing in inspiration and expiration is provided, as discussed in the following section.

## The Therapeutic Use of Pressure Breathing

A variety of clinical disturbances in respiration and circulation are treated with pressure breathing either in conjunction with administration of therapeutic gas mixture or with air itself. The indications and physiological effects of application of pressure in inhalational therapy will be considered under the following subdivisions: (1) continuous pressure breathing, (2) expiratory pressure breathing, (3) intermittent inspiratory pressure breathing, (4) equalizing pressure respiration with or without constant lung volume and with or without mechanically induced coughing.

### Continuous Pressure Breathing

Continuous pressure breathing refers to the application of a relatively constant pressure above the atmosphere approximately equal during inspiration and expiration during the inhalation of air or a therapeutic gas mixture. Its main uses are in the treatment of asthma, constrictive lesions in the larynx or trachea and pulmonary edema. In obstructive dyspnea the negative intrapleural and intra pulmonary pressure becomes pathologically elevated during inspiration mirroring the increased effort required to inhale air past the point of constriction in the respiratory passageway. The inhalation of an atmosphere under increased pressure results in decreased inspiratory effort, which is revealed by an immediate lowering of the intrapleural negative pressure during the inspiratory cycle. The maintenance of a similar pressure during expiration results in an increased volume of air in the lungs and widening of the lumen of the bronchi and bronchioles, thus diminishing constriction of the respiratory tract in respiration.

The return of blood to the right heart is retarded depending upon the mean pressure applied to the lungs. The venous pressure is elevated in normal subjects about 40 per cent of the applied intrapulmonary pressure, the remaining 60 per cent of the mean pressure used is absorbed by the lungs, chest wall and diaphragm, which at the end of inspiration constitutes the relaxation pressure of the chest that accomplishes expiration. In patients with pulmonary congestion due to heart failure the rise in venous pressure may be 60 to 70 per cent of the applied pressure, reflecting the diminished elasticity of the lungs under these circumstances. In patients with cardiac insufficiency damming back of blood into the peripheral circulation is an advantage since it allows the heart to cope with a smaller volume of blood. This is of special importance in the treatment of pulmonary edema; in addition an increased intrapulmonary pressure is exerted on the pulmonary capillaries only part of which is compensated for by an increase in right auricular and pulmonary capillary pressure. It would seem likely that the pulmonary capillaries are relatively compressed under these circumstances, thus decreasing the tendency of serum to leak outward.

Continuous pressure breathing should be administered cautiously in shock since the impairment in cardiac output may be made worse by interfering with venous return. If an urgent indication for pressure breathing exists, such as pulmonary edema, small increases of pressure such as 2 to 3 cm of water may be given if plasma or blood is administered at the same time. The blood pressure should be followed at 15 minute intervals in patients with peripheral circulatory failure and pressure employed should be reduced or discontinued if a fall greater than 10 mm Hg takes place in the systolic pressure during application of pressure breathing.

Pressure breathing is used in aviation medicine at high altitudes in which pure oxygen is inhaled in order to increase the partial pressure of oxygen dissolved in the plasma. A decrease of cardiac output of 20 per cent has been found in normal individuals who breathe pressures of 20 cm of water or above. However, in clinical practice a continuous pressure in the mask (or hood) of 4 to 6 cm is generally adequate for the treatment of obstructive dyspnea and edema of the lungs. When the condition of the patient is improved the pressure is very gradually reduced, 1 cm every two to three hours, in order to prevent a sudden inlet of blood into the right heart or perhaps return of dyspnea or edema. When pressures of 6 cm are employed the circulation time is prolonged especially in circulatory failure and the record of the ballistograph shows definite although slight decrease in cardiac impact. Pressure breathing is used in conjunction with 40 to 50 per cent oxygen or with 20 to 30 per cent oxygen with the diluent gas helium, the latter being especially helpful in asthma and in constrictive lesion of the larynx and trachea.

The methods employed include a positive pressure hood and a mask apparatus that makes use of weights on two rubber bags into which the therapeutic gas mixture is admitted. When a distensible rubber bag is available continuous pressure breathing

may be simply obtained not only in expiration but in inspiration also as a result of the elastic recoil of the collecting bag

### Expiratory Pressure Breathing

Expiratory positive pressure breathing permits inspiration at atmospheric pressure with expiration against a resistance which increases the intrapulmonary pressure only during the expiratory cycle. The use of this device is primarily for the treatment of edema of the lungs and for the administration of helium-oxygen mixtures in patients with bronchial asthma. Expiratory positive pressure is also employed after tracheotomy to combat the increase in seromucoid exudate that follows relief of laryngeal obstruction. Since pressure is not present during inspiration the effect on cardiac output is much less marked than in continuous pressure breathing although retardation of blood flow into the right heart takes place during the expiratory cycle with pressures of 4 to 5 cm of water.

The Meter mask is used with a metal disk which surrounds the expiratory flutter valve and contains on its external surface five orifices of different diameters. With the largest opening expiration proceeds without pressure; as the disk is turned to the smaller orifices the patient exhaled under an increased pressure of 1 to 4 cm of water or more depending upon the volume of breathing. A more accurate control of pressure may be obtained if the exhaled air is conducted through a water bottle calibrated in centimeters of water. The expiratory pressure Meter mask apparatus is the most convenient of the methods in use for the treatment of edema of the lungs either due to pneumonia left ventricular failure shock or irritant gas poisoning. Pressures of 4 to 5 cm of water are first employed and then gradually lowered when the signs of serous exudate in the lungs have disappeared. The rubber collecting bag is kept distended by administration through the injector attached to the regulator of 40 to 50 per cent oxygen at a flow of 12 to 15 liters per minute

### Intermittent Inspiratory Pressure Breathing

Intermittent inspiratory positive pressure consists of the administration of pressure which automatically inflates the lungs during inspiration expiration occurring either as a result of the relaxation pressure of the lungs and chest wall or mechanically by means of a negative pressure induced during the expiratory cycle; respirators of the latter type are known as suck and blow resuscitators. These apparatuses are used for respiratory failure due to a depressed or inadequate respiratory stimulus as in such conditions as poisoning with barbiturates morphine carbon monoxide alcohol as well as in drowning certain types of coma poliomyelitis with respiratory paralysis and electrocution.

When artificial respiration is employed especially with stuporous or unconscious subjects special attention must be given to clearing the respiratory passageway of mucus or other foreign matter by appropriate suction. The tongue is kept well forward and the head and neck maintained in extension with the chin somewhat elevated. When bronchospasm or pulmonary edema is present the inhalation of nebulized bronchodilator and broncho-vasoconstrictor drugs during the administration of intermittent pressure breathing may be found useful.

The effect of intermittent pressure breathing on the circulation is dependent upon the mean pressure employed. With apparatus in which the lungs are inflated by a positive pressure of 10 to 14 mm Hg with the pressure falling gradually to the atmosphere as a result of elastic recoil of the lungs and chest wall the mean pressure varies from 3 to 6 mm Hg depending upon the shape of the pressure curve. Interference with cardiac output may then take place under the circumstances previously described.

A similar effect on the circulation is produced by the tank type of respirator in which a negative pressure is created within the chamber achieving a gradient of pressure from the atmosphere into the lungs similar to that maintained by inspiratory positive pressure applied with a mask. In each instance the rise in venous pressure has been

found to be similar provided the mean pressure is the same When intermittent pressure breathing is used by an apparatus which provides a swift expiration and a long expiratory pause, the mean pressure is smaller and hence the effect on venous pressure and cardiac output is less Intermittent inspiratory pressure breathing is useful in the treatment of pulmonary edema in unconscious subjects but it is not generally helpful for the dyspnea of conscious patients who often require a higher velocity of air flow during inspiration than is provided by respirators now available In patients in whom peripheral circulatory failure is present the use of the positive and negative pressure (suck and blow) respirator appears to be preferable because they are effective and safe to use with unconscious subjects and the mean average pressure being near zero, produces no retardation of venous return and no impairment of cardiac output There is no convincing evidence that these forms of apparatus have deleterious effects on the lungs In all types of artificial respiration apparatus rapid tripping indicates that oxygen or air is not reaching the alveoli because of some obstruction

In respiratory paralysis the tank respirator may be used with a negative pressure of minus 15 to minus 20 cm of water and with a positive pressure within the tank of plus 5 to plus 8 cm instead of the entire pressure being employed on the negative side The effective mean positive pressure gradient would then be lower which would be of value in patients with circulatory failure High negative pressures within the tank being similar to high inspiratory positive pressure applied with a mask effective ventilation may be in some cases aided by adding an increase in intra tank positive pressure In this way anoxia and respiratory acidosis may be prevented without an undue blockage of venous return In current studies a swiftly opening valve has been attached to the tank respirator in which the pressure drop from minus 45 cm of water within the tank to the atmosphere takes place in 0 06 seconds, which results in a low mean pressure and has been shown to facilitate the elimination of bronchial secretions by increasing the velocity of air leaving the lungs during expiration, as a result of the relaxation pressure of the chest being exerted without hindrance from a gradually decreasing negative tank pressure

## Equalizing Pressure Respiration With or Without Constant Lung Volume and With or Without Mechanically Induced Coughing

Pressure respiration with a constant lung volume is provided by a chamber in which the patient is completely enclosed and exposed to a swift variation in air density by which an adequate pulmonary ventilation is achieved without necessity for voluntary respiration or chest movement An alternating pressure of 100 mm Hg thirty times a minute is provided by air entering and leaving the head end of the chamber from a motor blower or compressor unit A collar that partially surrounds the neck of the patient functions as a baffle reducing and delaying the air pressure wave to the outer chest wall to the same degree that the tracheobronchial tree exercises a resistance to air entering the alveoli and hence the inner surface of the thorax Similarly the wave of positive and negative pressure is exerted simultaneously and with equal force on the upper and lower surfaces of the diaphragm

Although patients may breathe freely in a chamber of this kind because there is no gradient of pressure difference between the inner surface of the lungs and the prevailing atmospheric pressure the chamber has been made use of for the treatment of pulmonary tuberculosis by training the patient to dispense with voluntary breathing and therefore with chest movement A normal pulmonary ventilation or an increased ventilation of the lungs may be continuously maintained by this method even in the presence of respiratory paralysis or a certain degree of obstruction in the respiratory passageway In recent studies the dyspnea of patients with bronchial asthma and pulmonary emphysema have been found to be promptly relieved a few seconds after equalizing pressure respiration has been accomplished Patients with orthopnea of moderate degree due to congestive heart failure have also

been able to lie supine without the sensation of shortness of breath

When patients suspend voluntary breathing a striking mental and physical relaxation takes place The output of potassium in the urine is diminished and the serum potassium is elevated during residence in the chamber which suggests that the adrenal gland is under less stimulation than normal The cardiac impact as measured by the Dock ballistocardiograph may be reduced 30 per cent below the level obtained at ordinary bed rest The pulse and blood pressure are lowered and the T wave in the electrocardiogram is slightly elevated The physiological effects noted point to a sharp decrease in oxygen consumption and general metabolic work incident to not only the diminished energy due to cessation of respiratory movement but largely to the mental and physical quiet which this form of ventilation without chest movement induces

In current investigations the chamber is being employed in patients with respiratory paralysis The ability to breathe at will without the imposition of the negative pressure in the tank respirator may prove to be helpful to patients with bulbar poliomyelitis both during the acute stage of the disease and later when attempts are made to accustom the patient to breathe without the respirator

A modification of this chamber has been made in which a mechanically induced cough is provided The head end of the chamber is connected to a valve which opens at the peak of the positive pressure cycle in 0 012 seconds which results in a high velocity of air leaving the lungs At the same time the baffle is closed tightly around the neck to produce a differential pressure of 40 mm Hg on the abdomen and chest wall In this way the human cough is simulated since the levator rib muscles hold the chest from expanding when the glottis is suddenly opened at the end of inspiration The momentary application of pressure to the abdomen is transmitted to the diaphragm this appears to be of crucial importance in eliminating mucus and purulent material in patients with bronchiectasis bronchial asthma and respiratory paralysis Preliminary clinical trials on human subjects and experiments on animals suggest that a mechanically induced cough may be of value in those clinical entities in which bronchial secretions are not gotten rid of because of impairment in the neuromuscular mechanism responsible for an effective human cough

## The Inhalation of Bronchodilator and Antibiotic Aerosols

Nebulization of bronchodilator and antibiotic drugs has been employed with the purpose of depositing these drugs in high concentration on the respiratory passageway and in the alveoli The site of deposition and absorption from the respiratory tract of therapeutic aerosols is dependent upon a number of factors especially the size of the droplets in the mist Particles of small size such as 0 3 to 0 8 micron in radius pass readily through the tracheobronchial tree to the alveoli where 60 to 70 per cent of them are absorbed depending upon the nature of the substance However particles of relatively large size such as 10 to 30 microns in radius are mostly precipitated on the pharynx larynx and trachea

In the treatment of bronchospasm it is preferable to employ a nebulin of bronchodilator solution of relatively small particle size such as 1 to 3 microns in radius in order to obtain both local application to the bronchioles and also absorption from the alveoli into the blood stream Solutions of 1 per cent epinephrine to 2 25 per cent racemic epinephrine are employed for quick relief of wheezing in patients with bronchial asthma and pulmonary emphysema Isopropyl adrenalin neosynephrin and at times atropine and sodium nitrate are also used in a nebulizer to produce vasoconstriction and bronchodilatation

In the treatment of bronchopulmonary infections with penicillin and other antibiotic aerosols deposition of the drug on the surface of the bronchial mucous membrane in a high local concentration is accomplished The sputum levels of penicillin when mists of a particle size between 1 and 3 microns in radius are inhaled are high in contrast to the absence of the drug when given intramuscularly Penicillin aerosol has been especially useful in the treatment of bronchiec

tasis in which more effective control of infection may be maintained by this method than by systemic administration. In inoperable advanced cases of bronchiectasis maintenance therapy of aerosol penicillin results in continued control of infection with, at times, remarkable relief of dyspnea and chronic infection. Penicillin resistant organisms are infrequently encountered with the exception of the hemolytic staphylococcus aureus but these resistant organisms may generally be eliminated by temporary marked increase in the dosage of penicillin aerosol.

In the treatment of acute and chronic in*fectious sinusitis aerosol penicillin has been* used in conjunction with the intermittent application of negative pressure to the nasal passages. In this way penicillin has been deposited in the accessory sinuses, at times with marked therapeutic benefit. The sulfonamide aerosols are also employed but have been largely superseded by penicillin and streptomycin. Streptomycin aerosol has been used in Friedländer B infections and in the treatment of bronchial and laryngeal tuberculosis in conjunction with parenteral administration of streptomycin. The newer antibiotic drugs terramycin aureomycin and chloromycetin do not lend themselves to aerosol administration because it is not as yet possible to give them in high enough concentration without irritation. However their administration by mouth or intravenously is especially valuable in overcoming infections with most resistant strains especially the Friedländer bacillus.

Penicillin aerosol has also been found to be of value in lung abscess and in chronic bronchitis refractory to intramuscular administration of the drug. Although originally used in the treatment of asthma and pulmonary emphysema in cases in which bronchial infection was present the incidence of increased bronchospasm is the physical result of the mist now makes it preferable to treat these conditions with systemic penicillin or with the newer antibiotic drugs.

Inhalation of penicillin and streptomycin in powdered form is less effective and more wasteful than by aerosol. Furthermore severe local reactions in the pharynx as well as serious bronchospasm in patients with asthma may be produced by penicillin administered as a dust. Although the inhalers available are convenient the clinical results are less good and the expense of continued use greater than effective administration of aerosol penicillin.

For the treatment of infections of the smaller bronchi a nebulizer is selected that produces particles of relatively small size such as 1 to 3 microns in radius, for the treatment of sinusitis a nebulizer that creates large-size particles is preferable in order to have a greater deposition on the nasopharyngeal mucous membrane and by use of *intermittent negative pressure* in the nasal accessory sinuses themselves. With adequate dosage and proper technique antibiotic aerosol therapy may result in marked benefit in the *clinical entities* for which aerosol therapy is intended such as bronchiectasis chronic bronchitis without bronchospasm sinusitis and lung abscess.

## REFERENCES


Andrews A H Manual of Oxygen Therapy Techniques Including Carbon Dioxide Helium and Water Vapor Chicago Year Book Publishers 1943

Ansbro F P Positive Pressure Respiration in the Treatment of Acute Pulmonary Edema Am J Surg 1945 *68* 185

Barach A L Physiologically Directed Therapy in Pneumonia Ann Int Med 1942 *17* 812

——— Physiologic Therapy in Respiratory Disease Philadelphia J B Lippincott 2 ed 1948

Barach A L and Richards, D W Jr Effects of Oxygen Therapy in Congestive Heart Failure Arch Int Med 1931 *48* 325

Barach A L Fenn W O Ferris E B and Schmidt C F The Physiology of Pressure Breathing A Brief Review of Its Present Status J Aviation Med 1947 *18* 73

Bickerman H A, and Beck G J Pressure Breathing With Oxygen and Helium Oxygen in Pulmonary Edema and Obstructive Dyspnea Bull New York Acad Med 1950 *26* 410

Boothby W M Mayo C W and Lovelace W R Jr Use of Oxygen and Oxygen helium With Special Reference to Surgery S Clin North America 1940 *20* 1107

Comroe J H and Dripps R D Physiologic Basis of Oxygen Therapy Springfield Charles C Thomas 1950

Comroe J H Jr Dripps R D Dumke P R and Deming M Oxygen Toxicity Reprinted With Additions from J A M A 1945 *128* 710

Cardon, I., Lemberg, I., and Greenbaum, R. S.: Bronchitis and Bronchiolitis in Pulmonary Disease. Ann. Int. Med. 1951 34 510

Eastman, N. J., Dunn, R. B., and Kreiselman, J.: Relative Value of Pure Oxygen and of Carbon Dioxide Mixtures in Experimental Resuscitation. Am. J. Obst. and Gynec. 1938 36 571

Effective Standards of Inhalational Therapy. Public Health Committee, New York Acad. Med. 1950 1,, 2,

Carthwaite, B., and Barach, A. L.: Penicillin Aerosol Therapy in Bronchiectasis, Lung Abscess and Chronic Bronchitis. Am. J. Med. 1947 3 261

Gordon, A. S., Fainer, D. C., and Ivy, A. C.: Artificial Respiration. J.A.M.A. 1950 1,, 1"

Kety, S. S., and Schmidt, C. F.: The Effects of Active and Passive Hyperventilation on Cerebral Blood Flow, Cerebral Oxygen Consumption, Cardiac Output and Blood Pressure of Normal Young Men. J. Clin. Investigation 1946 25 107

Levy, R. L., and Barach, A. L.: The Therapeutic Use of Oxygen in Coronary Thrombosis. J.A.M.A. 1930 94 1363

Motley, H. L., Cournand, A., Werko, L., Drysdale, D. T., Himmelstein, A., and Richards, D. W., Jr.: Intermittent Positive Pressure Breathing. A Means of Administering Artificial Respiration in Man. J.A.M.A. 1948 13 370

Poulton, E. P.: Local Tissue Anoxia and Its Treatment. Lancet 1939 30,

Richard, D. W., and Barach, A. L.: Prolonged Residence in High Oxygen Atmosphere. Effects on Normal Individuals and on Patients With Chronic Cardiac and Pulmonary Insufficiency. Quart. J. Med. 1934 3 427

Segal, M. S.: Inhalational Therapy in Treatment of Serious Respiratory Disease. New England J. Med. 1943 9 235

———: Severe Bronchial Asthma. Springfield, Ill., 1950, Charles C Thomas.

Thompson, S. A., and Birnbaum, G. L.: Pulmonary and Blood Gas Studies in Experimental Asphyxia and Asphyxial (Anoxia) Resuscitation. Comparison of Methods of Resuscitation. J. Thoracic Surg. 1942-43 12 607

Whittenberger, J., and Sarnoff, S. J.: Physiologic Principles in the Treatment of Respiratory Failure. Med. Clin. North America 1950 3, 1335-62

Wickner, I.: Combined Helium and Epinephrine Therapy. Ann. Allergy 1945 3 187


## ANTIMICROBIAL THERAPY

By H. Corwin Hinshaw, M.D.

The term *antimicrobial therapy* is receiving wide acceptance as a more inclusive and correct expression than *chemotherapy* or *antibiotic therapy*.

The most spectacular accomplishments in the field of antimicrobial therapy have been witnessed in the treatment of diseases of the respiratory tract.

*Therapeutic Objectives of Antimicrobial Therapy.*—The administration of specific drugs in infectious diseases of the respiratory tract is usually directed *toward retarding* the growth of the invading microbes, less frequently toward killing the microbes. Sometimes, as in pneumococcal pneumonia, inhibition for only a few days is sufficient to permit sufficient marshalling of the patient's defensive and reparative powers to lead to permanent healing. Sometimes, as in pulmonary tuberculosis, suppressive therapy must be continued for weeks or months before the disease can be arrested, and mechanical therapeutic aids are usually required. Sometimes, as in bronchiectasis, antimicrobial therapy is merely palliative and plays little part in effecting permanent arrest or cure of the disease. A logical approach to treatment would require the physician to define his therapeutic objective, guard against any possibility of unsatisfactory *progress toward it, and be prepared to modify* therapy as necessary.

It is unwise, however, to delay the treatment of fulminating disease until the bacteriologist verifies the physician's tentative etiologic diagnosis. *Frequently* the empirical use of penicillin has effected virtual cure before accurate bacteriologic and radiologic diagnosis has been achieved.

*The Pneumonias.*—*See* Chapter 5.

### Pulmonary Abscess

The therapeutic objective should be to treat each acute pulmonary infection with antibacterial agents adequately and before pulmonary abscess has developed. After necrotic processes have destroyed pulmonary parenchyma sufficiently to create an abscess cavity, the situation is so serious that prolonged illness and possible surgery are to be foreseen. However, a fair majority of pulmonary abscesses may be resolved by medical methods utilizing first penicillin and perhaps several antimicrobial agents in succession or in combination, if necessary, to control the infectious process. However

the factor of drainage is so important that antimicrobial therapy alone should not be depended upon without bronchoscopy, postural drainage, or, at times, surgical drainage Furthermore, it must be mentioned that bronchiogenic carcinoma, foreign bodies, bronchial strictures, bronchial adenomas, and rarer lesions may be the basis for any pulmonary abscess Interlobar empyema with bronchial fistula may simulate pulmonary abscess, and this was commonly seen before the day of virtually universal penicillin therapy in pneumonia

### Bronchiectasis

There is no definitive treatment for bronchiectasis except the radical surgical removal of all diseased pulmonary segments Before such operations the antimicrobial drugs are of great value in reducing the amount of purulent sputum and in improving the general condition of patients debilitated as a result of chronic pulmonary suppuration These drugs are of very great value in preventing the postoperative complications of empyema, postoperative atelectatic pneumonia and hematogenous dissemination of the infectious process (brain abscess, *etc* )

Inoperable bronchiectasis way offer insuperable obstacles which no amount or variety of drug therapy can surmount But dramatic results may be achieved by most intensive and prolonged efforts to control the *mixed bacterial infection largely responsible* for the distressing symptoms of the disease It is probable that the damaged bronchi never return to normal as a result of medical treatment but symptoms may be abated temporarily and when these recur as a result of reinfection, subsequent treatment may yield *similar results* However it is rarely observed that antimicrobial therapy can accomplish its goal without the most careful coordinated program of drainage and hygienic care

Penicillin and streptomycin have retained their popularity as the most practical agents in the treatment of bronchiectasis, and frequently the sulfonamides are worthy of trial Aureomycin, chloramphenicol and terramycin may be used for brief periods if well tolerated but these are seldom useful as the primary agents over prolonged periods

Penicillin and streptomycin may be administered by the aerosol method or by intramuscular injection or both The intramuscular method of injection offers some very *practical advantages, especially with* penicillin, but must be used with caution with *streptomycin because of the toxic* potentialities of the latter drug It is suggested that a trial period of intramuscular treatment with a mixture of penicillin (600,000 units daily) and streptomycin *(0 5 gm daily) be undertaken for a period of* approximately two weeks If hospitalization is feasible, it is well to utilize aerosol therapy simultaneously, but, if it is necessary for the patient to remain ambulatory aerosol treatment may be postponed until later

Aerosol therapy can never be administered *satisfactorily by means of the conventional* hand bulb as the source of motive power In hospitals an oxygen tank is most convenient and is always available It is equipped with a pressure-reducing valve and a flowmeter and is attached to a high-capacity glass nebulizer ( Vaponephrin ) with *a long length of rubber tubing It is more* economical to arrange a Y" connector to a by pass tube which will be closed with the patient s finger when he desires the nebulizer to operate during the inspiratory phase of respiration The nebulizer is charged by adding 1 cc of distilled water to the chamber, *and to this, a tablet of soluble crystalline* penicillin (50 000 units) is added and permitted to dissolve Streptomycin solution (100 to 200 mg in 0 5 cc water) may be added to counteract the Gram negative bacilli especially if these bacilli have been demonstrated on sputum smears The resultant solution may be nebulized and inhaled within 15 or 20 minutes It is suggested that this performance be repeated every one or two hours while the patient is awake Such intensive therapy is much more likely to be successful than a more leisurely program

It is advisable to save all sputum and note its character each day When the purulent component has disappeared the temporary goal has been achieved Frequent Gram stained smears of sputum will give an index

of the bacterial flora and it is especially important to do this if streptomycin is not being used When penicillin alone is used the Gram positive cocci frequently disappear promptly and are replaced by Gram negative bacilli of the coliform group The latter may disappear promptly when streptomycin therapy is added Sputum cultures are often less informative than simple smears of sputum stained by Gram s method

When the program described above has been adapted to the patient s needs and circumstances and given a good trial it may succeed in essentially sterilizing the tracheobronchial tree However such a happy state of affairs is not always realized When disappointment results it is well to try a course of treatment with aureomycin terramycin or chloramphenicol The dose tolerated readily will vary, but 0 5 gm four times daily is sufficient in some cases

Maintenance of a sterile tracheobronchial tree is of course an impossibility Maintenance doses of sulfonamide drugs (2 0 to 3 0 gm daily) may help to prevent or delay reinfection The usual cause of reinfection is an epidemic infection of the upper respiratory tract If penicillin is administered for a few days, reinfection may not occur

### Pulmonary Tuberculosis

In pulmonary tuberculosis antimicrobial therapy is most likely to be permanently effective against recently developed lesions lesions that have not progressed to necrosis The term *exudative tuberculosis* is frequently applied to lesions that have not yet caused marked lung changes and are therefore largely reversible Early tuberculous pneumonia and other types of extensive bronchiogenic or hematogenous pulmonary tuberculosis may be detected and treated effectively before coalescence of the numerous small foci has resulted in irreversible damage

Occasionally chronic indolent lesions of known long duration may retain a diffuse distribution and therefore be largely reversible but there is usually a close correlation between the age of a lesion and its reversibility However many large coalescent necrotic foci of pulmonary tuberculosis are surrounded by an extensive zone of disease which is capable of considerable resolution as a result of antibacterial drug therapy The central core of destroyed tissue will almost surely require collapse therapy or excision but resolution of the peripheral exudative component may be necessary to stem the progress of the disease and to permit effective mechanical treatment directed toward the central anatomical defect

It is difficult to determine the state of pathologic development of many lesions of pulmonary tuberculosis because the physician is so dependent upon radiographic methods of demonstration which are known to be fallible However experienced radiologists and physicians are becoming more adept at determining which shadows are likely to represent disease amenable to antimicrobial therapy

The mucosal complications of pulmonary tuberculosis which produce the distressing symptoms of tracheobronchial laryngeal oropharyngeal and intestinal tuberculosis often respond remarkably to antimicrobial therapy Such treatment is frequently justified merely to relieve symptoms even though the pulmonary disease may appear to be incurable Undoubtedly drug therapy may yield comfort and prolong the duration of life in many hopeless types of pulmonary tuberculosis

*Therapeutic Regimen* —Streptomycin (or dihydrostreptomycin) remains the most effective and most widely applicable drug for treatment of pulmonary and extrapulmonary tuberculosis but present-day practice is to recommend that it always be combined with para aminosalicylic acid (' PAS ) Several regimens are in common use the most widely accepted of which are listed below

(*1*) *Combined Intermittent Regimen* — Para aminosalicylic acid by mouth 12 0 gm or more daily (3 0 gm four times daily or 4 0 gm three times daily taken with food) and streptomycin (or dihydrostreptomycin) 1 0 gm intramuscularly every second or third day this is a regimen well tolerated by adult patients of average weight and is effective over prolonged periods

This regimen seldom yields the neurotoxic complications of streptomycin therapy The physician must recognize that though highly susceptible individuals may have some degree of loss of vestibular function after prolonged

the factor of drainage is so important that antimicrobial therapy alone should not be depended upon without bronchoscopy, postural drainage or, at times, surgical drainage Furthermore, it must be mentioned that bronchiogenic carcinoma, foreign bodies, bronchial strictures, bronchial adenomas, and rarer lesions may be the basis for any pulmonary abscess Interlobar empyema with bronchial fistula may simulate pulmonary abscess, and this was commonly seen before the day of virtually universal penicillin therapy in pneumonia

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Aerosol therapy can never be administered satisfactorily by means of the conventional hand bulb as the source of motive power In hospitals, an oxygen tank is most convenient and is always available It is equipped with a pressure reducing valve and a flowmeter and is attached to a high capacity glass nebulizer ("Vaponephrin") with a long length of rubber tubing *It is more* economical to arrange a "Y" connector to a by pass tube which will be closed with the patient s finger when he desires the nebulizer to operate during the inspiratory phase of respiration The nebulizer is charged by adding 1 cc of distilled water to the chamber and, to this, a tablet of soluble crystalline penicillin (50 000 units) is added and permitted to dissolve Streptomycin solution (100 to 200 mg in 0 5 cc water) may be added to counteract the Gram negative bacilli especially if these bacilli have been demonstrated on sputum smears The resultant solution may be nebulized and inhaled within 15 or 20 minutes It is suggested that this performance be repeated every one or two hours while the patient is awake Such intensive therapy is much more likely to be successful than a more leisurely program

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# Chapter 23

# Diseases of the Kidneys

By LOUIS LEITER, M.D., Ph.D.

DISEASES of the kidney occupy a special place in medicine because of the wide variety of symptoms and signs produced in their course, the seriousness of their complications and the sequelae in other organs and systems of the body.

## RENAL FUNCTION

The major function of the kidney is the elaboration of urine. This is a *homeostatic function* set to preserve a constant internal milieu—constant as to volume of body fluid, circulating or extravascular; as to electrolyte composition individually and in toto; as to osmotic pressure; as to acid-base equilibrium; as to the waste products of protein metabolism; and as to the important nutritional elements, such as glucose, amino acids and vitamins. In addition the kidney rapidly excretes a great variety of foreign substances, including therapeutic drugs—an important factor in effective blood levels and in possible accumulation of toxic amounts during renal impairment. The kidney is believed by some investigators (Grollman *et al.*) to exert a homeostatic effect on blood pressure. The normal absence of significant proteinuria acts as a protection for plasma volume and the dynamic equilibrium of fluid exchange between intravascular and extravascular fluids. In all these functions the kidney behaves on the principle of conservation of the normal pattern of body fluids. It begins with a general ultrafiltrate of the plasma in the glomerular fluid and by selection and rejection of ions and nonionic solutes (as well as by secretion of others either from the blood or by enzymatic manufacture within the tubular epithelium—ammonia, for example) finally produces the complex mixture known as urine. Urine differs widely from the blood plasma and other body fluids, yet represents a concentrate of all that the body does not need or should not retain from the metabolism of food or tissues.

GLOMERULAR FILTRATION.—Certain aspects of renal physiology deserve special emphasis in view of their importance in clinical diseases of the kidneys. The process of glomerular filtration takes place at relatively high pressure, thanks to the arrangement of the capillary tuft between afferent and efferent arterioles, the latter being of smaller caliber and higher tone or resistance than the former. Filtration also requires a large blood flow, or inspissation would soon put a stop to it. Normally about 25 per cent of the basal cardiac output of blood per minute flows through the kidneys. The glomerular filtration squeezes out about 17 per cent of the plasma. (In infants, especially premature infants, the glomeruli are not fully developed and filtration is much lower than one would expect from the body surface area. Hence the ease with which overhydration can be produced, or nonprotein nitrogen retention.) In any clinical situation involving a decreased cardiac output, as in heart failure or shock, renal blood flow is sharply reduced and filtration suffers. However, compensatory efferent arteriolar constriction may, in time, increase the fil-

treatment this seldom occurs except in patients with defective renal function severe enough to impair ability to excrete streptomycin The resultant high level of streptomycin in the blood and tissues may produce damage to either the vestibular branch or the auditory branch of the eighth cranial nerve

The appearance of strains of tubercle bacilli resistant to either streptomycin or PAS is greatly delayed when the above regimen is employed and treatment may be continued with cumulative benefit for from four to twelve months if necessary This regimen is chosen for treatment of patients with noncritical types of tuberculosis and is used when preservation of drug sensitivity appears to be most desirable

(2) *Combined Continuous Regimen* —Para aminosalicylic acid by mouth 12 0 gm or more daily and streptomycin (or dihydrostreptomycin) 1 0 gm intramuscularly once each day this is a regimen used extensively It is preferred for more critical types of pulmonary tuberculosis or more violent complications of pulmonary tuberculosis After symptomatic or radiographic improvement it may be desirable to change to the combined intermittent regimen the latter being more likely to prevent the appearance of drug-resistant strains of tubercle bacilli

(3) *Other Schedules of Treatment* —PAS may be utilized without a streptomycin drug when preservation of streptomycin sensitivity is of paramount importance as for example when radical surgical treatment is foreseen at a remote future date after months of preparatory medical therapy

In desperate clinical circumstances the amount of streptomycin recommended in previous paragraphs may be increased to 2 0 gm daily, but usually for limited periods of time only When such doses are continued for several weeks the patient usually suffers some degree of neurotoxicity

Streptomycin drugs should always be combined with PAS whenever the latter drug is tolerated in doses larger than 6 0 to 8 0 gm daily, because of the proved ability of PAS to delay the development of bacilli resistant to streptomycin It is probable that the two drugs exert an extra therapeutic effect against tuberculosis and that the rate of improvement is accelerated as the term of effective action is prolonged

Para aminosalicylic acid frequently gives rise to uncomfortable gastrointestinal irritation which restricts the amount of drug tolerated Several preparations of PAS and sodium PAS are available Frequently it is necessary to give a patient the preparation he prefers Enteric coated preparations especially enteric-coated tablets, may not be well absorbed Granules coated with a stearate preparation and flavored to increase palatability are fully absorbed Tablets of sodium para aminosalicylate are preferred by some patients and others prefer liquid mixtures of sodium PAS which have been flavored For example

℞ PAS 100 0 gm
Sodium bicarbonate 70 0 gm
Oil of peppermint 5 – 10 drops
Water q s ad 500 cc

After effervescence has subsided each 5 cc of this mixture will contain the equivalent of 1 0 gm of PAS as the sodium salt Liquid preparations of sodium PAS are not stable at room temperature but may be kept for a few days at refrigerator temperatures

*Other Antimicrobial Agents in Tuberculosis* —The thiosemicarbazone drugs especially amithiozone (also known as Tb 1 ) have attained considerable popularity in Europe, especially in Germany Most of the observations recorded at this time were made before the observers had had the opportunity of comparing this substance with the streptomycin drugs and PAS In the United States a large majority of physicians who have studied amithiozone have concluded that it is inferior in efficacy and much more toxic than are the streptomycin PAS regimens described above However tuberculosis is a disease so variable and so prolonged in its course that physicians may need more than two or three drugs for treatment of some types of the disease Therefore it is widely believed that the thiosemicarbazone drugs may be valuable adjuncts to the more effective and less toxic preparations The circumstances requiring such treatment are not well defined but some physicians believe that tracheobronchial tuberculosis may be especially responsive to amithiozone

As to the more complex tests, the *urea-clearance determination* has maintained its popularity in recent years. It has the advantage of furnishing a blood urea estimation, a measure of glomerular filtration and, in case of average or low urine volumes, an indication of the ability of the tubules to concentrate urine. The last is given by the concentration factor or $\frac{\text{urine urea}}{\text{blood urea}}$ ratio. Though the urea clearance on the average is about 60 per cent of the inulin clearance or true glomerular filtration rate, it fluctuates considerably due to variations in back diffusion of urea at different rates of urine flow. The various formulas for urea clearance attempt to allow for this, but it is safer to ensure a good diuresis. Incomplete emptying of the bladder (with corresponding inaccurate test results) must be expected without catheterization and this is another reason for encouraging a larger urine volume during the test. Urea-clearance figures may be grossly erroneous and deceptive in the presence of bladder or ureteral obstruction, but the concentration ratio will still be helpful. The urea clearance may also be affected by prerenal influences apart from those which influence the circulation directly and glomerular filtration secondarily. Thus, a very low protein diet may reduce both the blood urea and the urea clearance to lower or subnormal level. Since in chronic diffuse renal disease there is a simultaneous impairment of both glomerular filtration and tubular reabsorption, it is not surprising that there should be a fair parallelism in general between the urea clearance and the specific gravity test. *This applies only down to the level of about* 30 per cent of normal urea clearance, at which point the maximum specific gravity has usually become fixed at 1 010-1 014, the isosthenuria level of Volhard. Further decrease in renal function—finally, to the uremic level—is still measurable by the clearance tests but no longer by specific gravity changes. It is in this range that the urea clearance is very helpful.

The battery of *specific glomerular and tubular clearances* developed by Smith, Goldring and Chasis and the investigators who followed their pioneer work with infusion techniques have made it possible to determine specific glomerular and tubular functions as well as renal blood flow and other renal hemodynamics, with an amazing degree of certainty. Unfortunately, these are essentially research tests and require unusual skill on the investigator's part and a reasonable amount of endurance on the subject's. From the practical clinical standpoint these specific clearances and their derivatives (TmPAH or the tubular excretory mass, and Tm glucose or the measure of the number of functioning whole nephrons) have served chiefly as a standard of reference, an absolute yardstick against which the cruder measures of kidney function described above have been assayed and compared with the clinical data and pathologic findings in human renal disease and in experimental renal deficiencies. The great value of the specific clearances in elucidating the role of circulatory and other prerenal factors in renal functional impairment has been beautifully demonstrated in studies on shock, congestive heart failure, diabetes insipidus, adrenal cortical insufficiency and hyperfunction and a variety of other disturbances. As a result finer changes in renal function can now be used as indicators or mirrors of metabolic disturbances in important non renal conditions such as diabetes mellitus, hyperparathyroidism, pregnancy, muscular dystrophies, hepatic disease and gout.

*In renal diseases proper certain patterns of dysfunction* emerge as dependent on the degree of involvement of different portions of the nephron. For example, in glomerulonephritis, the glomerular filtration is generally reduced disproportionately to the changes in renal blood flow or functional tubular mass, at least in the earlier stages of the disease. This pattern is what one would expect from the pathology of the glomeruli. The ratios of $\frac{\text{GFR*}}{\text{RBF*}}$ FF*, $\frac{\text{GFR}}{\text{Tm}}$ are quite low. On the other hand $\frac{\text{RBF}}{\text{Tm}}$ may be supernormal, showing relative hyperemia

*GFR stands for glomerular filtration rate, FF for filtration fraction or $\frac{\text{GFR}}{\text{RPF}}$, RPF for renal plasma flow, RBF for renal blood flow, Tm for maximal tubular function, whether for excretion or reabsorption, as a measure of tubular mass.

tration fraction to two or three times the normal thus maintaining filtration at the cost of tubular blood flow If the glomerular membrane is seriously altered by disease as in glomerulonephritis or diabetic glomerulosclerosis filtration is severely reduced even though adequate blood flow may continue through the opaque capillaries The filter pores are clogged, so to speak, and extra flow or higher pressure may do little good It is also evident that if the pre arterioles or small renal arteries are diffusely narrowed filtration cannot be satisfactory even with normal cardiac output and blood pressure The same applies to a severe constriction of the main renal artery However, if the blood pressure should rise considerably, as in the Goldblatt hypertensive animal adequate filtration pressure may be propelled into the glomeruli in spite of renal arterial resistance at the expense of increased cardiac work and its ultimate consequences

TUBULAR REABSORPTION —Tubular reabsorption is normally geared to glomerular filtration This prevents undue reabsorption of water and electrolytes by tubules attached to smaller glomeruli or excessive loss by tubules connected with larger glomeruli This balance is regulated not merely by the nephron itself but is probably subject to posterior pituitary- and adrenal cortical hormone control of renal tubular activity The process of reabsorption along with tubular excretion and tubular secretion is vastly complicated because of its specificity its sensitivity to plasma levels of the particular solute, its localization in different segments of the tubule its dependence on enzyme systems and a high oxygen supply its definite limits or maxima (*e g* for glucose reabsorption p aminohippurate or diodrast excretion, and ammonia secretion) and its relative independence of the renal blood flow or glomerular filtration rate It is not surprising, therefore that in renal disease with varying involvement of different parts of the nephron, all sorts of functional patterns may be found on appropriate testing by modern clearance techniques In isolated instances, it is possible to determine that the major dysfunction is in the distal tubule For example, in cases of nephrocalcinosis with good glomerular filtration and fair Tm for glucose, but without ability to concentrate the urine, it is possible to show that the distal tubule fails either to form ammonia in response to the stimulation of acid ingestion or to produce a strongly acid urine

MEASUREMENT OF RENAL FUNCTION —This may be very simple or quite complex The simplest over all measures of renal function are (1) the maximum concentrating ability or specific gravity of the urine under the stimulus of a low fluid intake and (2) the nonprotein nitrogen or urea and creatinine levels in the blood The former is virtually a measure of tubular function, especially of distal tubular function, the latter involves the efficiency of glomerular filtration If one adds the phenol red or phthalein test (PSP) one also obtains a crude measure of renal blood flow and tubular function (from the first 15 minute excretion of dye in addition to the total during the first hour) It is apparent that even these simple tests are subject to the influence of prerenal or extra renal factors For example, the concentration test assumes that there is no extra fluid in the body, or edema which may counteract the supposed dehydration This is often not so in renal disease with gross or latent edema or obvious or early cardiac incompetence Furthermore unless the patient has a normal protein and salts intake the urine may not even under dehydration receive enough solid wastes to produce a high specific gravity Correction of the readings for low temperature, proteinuria, and glycosuria is essential for accurate interpretation and may yield strikingly abnormal results otherwise mistaken for those of normal function In the case of nonprotein nitrogen or urea in the blood the interpretation of abnormal values must take into account the influence of variations in dietary protein fluid intake and urinary output tissue protein catabolism as altered by infection or trauma and other prerenal factors Since creatinine reflects chiefly endogenous protein metabolism, its level in the blood when carefully determined is a much more reliable index of renal function, specifically of glomerular filtration

## PATHOLOGIC PHYSIOLOGY OF RENAL DISEASES

An understanding of the normal functions of the kidney, their mechanisms of activity and regulation by intrarenal and extrarenal influences, makes the disturbed physiology and much of the symptomatology of renal diseases readily intelligible. Let us consider some of the major manifestations of clinical renal disease—proteinuria, edema, oliguria and anuria, hypertension, renal insufficiency and uremia, and the less common but important renal osteodystrophy, previously known as renal rickets or renal dwarfism when it affected children.

## PROTEINURIA

Proteinuria, one of the most important signs of renal disease, represents an increased permeability of glomerular capillaries to plasma protein. Very slight damage to the glomerular membrane results in an escape of the smallest plasma protein molecules, the albumin fraction. More severe inflammation or vascular injury would permit larger protein fractions, the globulins of various sizes and finally even fibrinogen to leak through. In fact, in the relatively mild glomerular damage associated with the uncomplicated nephrotic syndrome 90 per cent or more of the urinary protein has been found to be in the albumin fraction; in severe subacute glomerulonephritis gamma globulin and fibrinogen appear in increasing proportions and furnish a serious prognostic sign, according to Blackman *et al*. This viewpoint does not exclude the possibility, championed by Dock, Addis and Oliver and others, that even normally a small amount of plasma albumin filters out from the glomerular capillaries under the high blood pressure in them and is almost entirely reabsorbed by the proximal convoluted tubule. It has been established by repeated infusion of homologous undenatured serum albumin in man and animals that albuminuria develops and increases roughly quantitatively with the rise in serum albumin concentration even in the presence of originally normal kidneys. This also suggests normal glomerular permeability to albumin. In renal disease the tubular reabsorptive mechanism for protein may be damaged primarily or become overloaded as a result of the increased protein content of the abnormal glomerular filtrate and thus permit much protein to escape into the urine. Even if only a few milligrams of protein per 100 cc of glomerular filtrate failed of reabsorption, the total amount of protein excreted in the urine in 24 hours might easily amount to several grams in view of the normal filtration rate of about 180 liters in 24 hours. This is precisely what must happen in the nephrotic child in whom the glomeruli are scarcely altered and exhibit a normal or supernormal filtration rate but in whom every glomerulus leaks a tiny amount of protein. The highest degrees of proteinuria are found in nephrotic children. In the more severe inflammatory glomerulonephritis with obstruction to filtration and in the later stages of nephritis with marked fibrosis and disappearance of functional glomeruli the proteinuria becomes much less significant because of the great reduction in filtering surface.

The *consequences of proteinuria* are readily apparent. Within the kidney itself the precipitation of the protein (due to changes in acidity and other factors in the evolving urine) leads to the formation of casts or moulds of the tubular lumina. These casts may at times produce obstruction of individual tubules or stir up an inflammatory reaction about them to the detriment of renal integrity and function. In the circulating plasma the albumin concentration eventually falls as the drain of albuminuria continues and as the replacement by regeneration of plasma protein fails ultimately to keep pace with the loss in the urine. Once *hypoalbuminemia* has developed to the point where the protein osmotic pressure no longer can balance the hydrostatic filtration pressure in the capillaries of the body and other factors in fluid exchange no longer can compensate, *nephrotic edema* will result if salt is available. Since a dynamic balance among various factors is involved, one should not speak of a "critical edema level" of plasma albumin. However, in the absence of abnormality in venous and capillary pressure or of lymphatic drainage, it is generally true

of the tubules in striking contrast to the situation in essential hypertension or in congestive heart failure, in which the tubules are relatively ischemic In both the latter diseases, FF* remains quite high (particularly in heart failure) due to excessive efferent arteriolar constriction This constriction tends to maintain glomerular filtration in spite of severe reduction in renal blood flow Yet in hypertension the $Tm_{PAH}$ falls as the disease progresses beyond the early stage and becomes a sensitive indicator of the renal functional status, on the other hand, in severe heart failure of rheumatic origin in adults without intrinsic organic renal disease or vascular changes the $Tm_{PAH}$ and the $Tm_{GLUCOSE}$ are usually perfectly normal This contrast in maximal tubular functions may also apply to the ability to reabsorb salt and have an important bearing on the problem of edema

The various functional patterns in glomerulonephritis and other renal diseases have been carefully studied and reported by Earle *et al*, by Corcoran Taylor and Page and others The greatest usefulness of specific renal function tests is in following the course of the disease in prognosis and in gauging the effects of therapy

It is ordinarily impossible to tell from the various clearance tests whether one or two kidneys are present or there is a difference in function between the kidneys especially if such a difference is due to obstructive lesions When the question of unilateral disease or dysfunction or obstruction must be decided the most practical method is *intravenous pyelography* in which advantage is taken of renal tubular excretion and high concentration of iodinated hippuric-acid compounds or related substances Under proper conditions one kidney s function may be compared with the other s However considerable impairment in bilateral function as indicated by a low urea clearance and elevated blood urea or creatinine will affect the diodrast excretion sufficiently to render intravenous pyelography useless In many instances cystoscopy and retrograde studies are eventually necessary The use of dyes such as phenol red or indigocarmine during the latter procedure is helpful provided due allowance is made for possible differences in urine volume from the two kidneys

## Diuresis

Diuresis is not a simple process, for it may involve glomerular, proximal tubular and distal tubular functions in varying degrees The simplest type is water diuresis or very dilute urine resulting from temporary disappearance of the posterior pituitary antidiuretic hormone from the blood In this type of diuresis, only the distal tubule seems to be involved, since it can separate salt from water reabsorb the former and discard the latter anisoosmotically On the other hand when hypertonic salt or glucose solution is injected intravenously and fairly rapidly or the filterable but not reabsorbable inulin, mannitol, or sodium thiosulfate is injected in appropriate amounts marked diuresis results but it is different from water diuresis It is an osmotic diuresis due to concentration of an unreabsorbed solute in the tubular fluid with prevention of normal water reabsorption because of the energy limits of the renal tubule Sodium chloride potassium and other normal electrolytes may be washed out in the process which if severe enough may cause considerable depletion This osmotic diuresis acts all along the tubule proximal and distal The stimulating effect of intravenous injection of hypertonic solutions may also increase cardiac output renal blood flow, and glomerular filtration and so contribute another element to diuresis Finally diuresis can be produced by drugs like the mercurials by their toxic action on proximal or distal tubular function The mercurials reduce the normal reabsorbing capacity for salt and water and allow more to escape into the final urine Purine diuretics also have this effect but may also briefly increase cardiac output renal blood flow, and glomerular filtration The relative independence of water diuresis from renal blood flow and filtration in man is illustrated in the response to a high fluid (salt free) intake in patients with severe congestive heart failure

## OLIGURIA AND ANURIA

*Oliguria* exists in the adult when the daily urine volume falls to 500 cc or less. Ordinarily this is the result of inadequate intake of fluids or excessive extrarenal loss, with secondary mobilization of antidiuretic posterior pituitary hormone (which increases renal tubular reabsorption of water and produces a concentrated urine). Among the direct renal causes of oliguria are (1) decreased *glomerular filtration with more complete* tubular reabsorption of the provisional urine, whether due to glomerular inflammation, circulatory renal ischemia, intrarenal edema, or obstruction to urinary flow, and (2) toxic nephrosis with back-diffusion of filtrate through damaged or necrotic tubular epithelium. Prerenal deviation of fluid in the form of edema or ascites is an important cause of oliguria. Pain arising in the urinary tract may set up reflex oliguria by way of vasomotor changes *in renal blood flow or* release of antidiuretic hormone. Pituitary antidiuretic hormone secretion may also be increased by the action of morphine, barbiturates and other drugs. When oliguria is due to extrarenal factors and the kidneys are normal, the urinary specific gravity and color are high. The association of oliguria and a low specific gravity—less than 1.020—speaks for renal damage, whether of organic or functional origin. The occurrence of oliguria with specific gravities of from 1.010 to 1.016, approximately isotonic with glomerular filtrate, indicates severe renal functional impairment. Because of *its frequent dependence on dehydration* oliguria is commonly associated with a variety of electrolyte disturbances. Determination of the nature of electrolyte imbalance is essential for good treatment.

*Anuria* exists whenever the daily urine volume is less than 100 cc. Retention in the bladder must be excluded. Anuria is one of the most dangerous medical situations and nearly always signifies severe acute organic disease or poisoning of the kidneys, bilateral ureteral obstruction or vascular occlusion, prolonged circulatory or hemolytic shock, urinary extravasation or surgical removal of the only functioning kidney. The consequences of anuria and their treatment are described in the sections on uremia and the toxic nephroses. The vital importance of an early diagnosis of anuria and determination of its etiology is obvious.

## HYPERTENSION

Elevation of arterial blood pressure, systolic and diastolic, is a common manifestation in most of the organic renal diseases and in certain of the renal dysfunctions. The secondary effects of persistent hypertension on the cardiovascular system, including the renal arteries and arterioles, may be far more serious in time than the renal excretory insufficiency caused by *the progression of* the original disease. There is no relationship between the degree of renal excretory impairment and the level of arterial blood pressure. (*see* Chapter 24.)

## RENAL INSUFFICIENCY

*Retention of non-protein nitrogen* in the blood is a major sign of renal functional impairment and reflects reduction in glomerular *filtration*, *whether caused by organic* changes in the kidney or by altered renal hemodynamics secondary to circulatory shock or depletion of varied etiology. Of course, retention of nitrogenous metabolites may also result from obstruction anywhere in the kidney or post-renal urinary passages. The rate of accumulation of non-protein nitrogen in any case is largely determined by the numerous factors affecting protein catabolism. A high exogenous supply of protein in diet or parenteral infusion will exaggerate the degree of non-protein nitrogen retention unless the body has been severely depleted of protein and stores most of the administered nitrogen.

Similarly, high blood NPN levels will develop if trauma, surgery, infection or neoplastic disease with high fever, uncontrolled diabetes, or other reason for increased endogenous protein catabolism are superimposed on renal impairment. Yet renal function may be basically unchanged from its original level. Given a constant level of renal functional impairment, a constant rate of protein catabolism (whether of exogenous or endogenous protein), there may still be considerable fluctuations in the blood NPN concentration due to the simple and often ignored fact that the *urinary output of nitrogen wastes is partly de-*

that, in the adult, it is rare to see edema on a nephrotic base when the plasma albumin is above 2 5-3 0 grams per cent It is rare, on the other hand, not to see it when the plasma albumin is below these values if salt is given with the diet or the subject is ambulatory or is not receiving diuretic drug therapy All of this discussion of hypoalbuminemic edema assumes renal tubules capable of at least normal reabsorption of salt *If they are so damaged as to allow filtered salt to pass through them in a percentage higher than normal, the patient's problem* becomes no longer one of edema but of possible salt depletion The combination of massive proteinuria hypoproteinemia and tubular insufficiency for reabsorption of salt is virtually impossible for the first of these is rare when renal disease is so severe as to have produced the last

## EDEMA

Edema in renal disease is far more complex than the relationship between proteinuria and low plasma albumin and its osmotic pressure Within the kidney itself there is the balance between glomerular filtration and tubular reabsorption of salt a balance *entirely different from the Starling mechanism operating on a purely physical level in the general peripheral capillaries* If glomerular filtration is more impaired, absolutely or relatively in glomerulonephritis than the tubular reabsorbing function is it is easy for more complete reabsorption of salt and water to take place because of the smaller amount of filtrate Therefore the glomerulo tubular imbalance produces retention of salt and edema On the other hand when glomerular filtration is normal in young nephrotic edematous children, one must assume an actual increase in tubular reabsorption of salt beyond the normal range Here we see possible extrarenal influences on tubular reabsorption of salt, or sodium Both the antidiuretic hormone of the posterior pituitary and the adrenal cortical salt retaining steroids have been implicated There may well be other factors Certainly, the low plasma volume so constantly found with hypoalbuminemia due to proteinuria must bring into counterplay powerful compensatory mechanisms Ultimately, these must act on the nephron The kidney's excretory function is only a means to an end—conservation of body fluid and circulating volume, with proper electrolyte make up A low plasma volume however produced, should somehow act as a powerful stimulus to retention of salt and water by the kidney, even though this fluid should promptly leak out into the tissue spaces and result in edema

Apart from nephrotic edema, there are at least three other kinds of edema seen in certain renal disorders The *edema of acute nephritis* is partly due to toxic changes in *capillary permeability ascribed to the precipitating hyperergic reaction* and partly to the glomerulotubular imbalance described above In fulminating acute nephritis or *toxic nephrosis with early severe oliguria* or anuria *edema* may be a *purely mechanical* retention of excess fluids not otherwise disposable either because of virtually absent *filtration in the glomeruli or complete back* diffusion of reduced filtrate through necrotic or completely *permeable tubular walls* no longer reabsorbing or excreting selectively In both the acute and more commonly the chronic hypertensive stages of renal disease *edema* may result *from heart failure* This introduces a vicious circle since the circulatory dynamics of congestive heart failure of whatever etiology include a marked reduction in renal blood flow and glomerular filtration and corresponding defects in salt excretion and other renal functions The effects of these added handicaps on a diseased kidney are serious and difficult to counteract

One more factor of importance for both proteinuria and edema deserves mention This is *elevation of renal venous pressure* as seen ordinarily in congestive heart failure with high systemic venous pressure Proteinuria oliguria salt retention and *edema* are usually associated with severe passive congestion of the kidney *The presence of* ascites under pressure aggravates the venous disturbance in the kidney *by direct* hydrostatic effect on renal venous outflow

stages of renal diseases organic or functional *Phosphate* is also retained in severe renal insufficiency but in a much more complex manner than sulfate because of the numerous metabolic energetic processes in which phosphate is involved Furthermore the level of phosphate in the blood even with poor renal function is held in check by the precipitation of insoluble calcium phosphate which is somehow removed from the circulating blood in some colloidal form Phosphate retention also contributes to metabolic acidosis besides playing havoc with the serum calcium which is reciprocally reduced *Calcium* in addition tends to be lost in excess by poorly functioning renal tubules Hence it never accumulates in the blood in renal disease unless another factor enters—increased mobilization from bone by osteolytic disease chronic acidosis hyperparathyroidism or other hormonal disturbance vitamin D intoxication or severe immobilization of the body In these situations the flood of calcium reaching the kidneys is more than they could handle even if they were normal and precipitation of calcium phosphate within the parenchyma of the kidneys adds injury to insult creating a vicious cycle

Retention of *potassium* may occur in renal insufficiency but rarely to dangerous levels in the absence of oliguria or anuria Potassium is normally excreted by filtration and reabsorption with the difference from sodium that its excretion continues regardless of the need of the body for potassium during states of cellular depletion However should the serum level become abnormally high potassium is then actually excreted or secreted by the renal tubule as shown by the urinary potassium which exceeds the amount of potassium filtered The ability of potassium to enter cell water its participation in carbohydrate metabolism and other activities as well as its toxic effects on the heart and other muscles place it in a special category In renal insufficiency without severe oliguria low serum potassium levels may develop after prolonged vomiting diarrhea or diuresis in the presence of a low intake of potassium-containing food Since serious symptoms may arise from either high or low extracellular potassium concentration accurate measurement of serum levels is essential for proper therapy *See* Chapter 14

*Chloride* like sodium is so largely retained by the normal kidney that it would not be expected to increase in the blood in renal decompensation Furthermore loss by vomiting common in uremia is often a cause of considerable reduction in serum-chloride concentration Also the accumulation of other anions (*e g* sulfate and ketone acids) may displace not only bicarbonate but even chloride in extracellular fluids The entrance of choride into cellular water in various metabolic derangements is also believed to occur However the serum-chloride level may rise in renal insufficiency in the absence of vomiting or other extrarenal loss and produce a chloride acidosis by lowering the bicarbonate concentration even in the presence of a normal sodium value The reason for this chloride retention probably lies in the fact that the renal tubule normally has to excrete relatively more chloride than sodium for in all extracellular fluids the normal ratio of sodium to chloride in milliequivalents is roughly 150 100 or 3 2 whereas in ordinary salt as ingested the ratio is 1 1 This means that the kidney must always dispose of more chloride ion than sodium ion in order to keep the ratio in body fluids 50 per cent higher than it is in sodium chloride In certain types of tubular damage in renal diseases this selective function may be seriously impaired and chloride accumulate in the blood and all other fluids in equilibrium with it Serum chloride and sodium may both be elevated strikingly in certain diarrheas of infancy with severe dehydration and functional renal disturbance or in the rare cases of sulfathiazole or sulfadiazine nephrosis and encephalopathy in which parenterally administered saline is largely retained but water is lost from the skin as the result of high temperatures leaving hypertonic salt behind (Luetscher and Blackman)

The serum bicarbonate concentration in renal insufficiency may be normal but is generally reduced in varying degrees owing to the accumulation of other anions all of which are stronger acids than carbonic acid and therefore displace bicarbonate from its sodium partner If loss of acid gastric juice by vomiting has occurred the bicarbonate may return only to a normal level from a previously low value and still be associated with a considerable alkalosis because of the increase in ratio of bicarbonate to free carbonic acid This possibility must be borne in mind whenever the serum sodium is normal in the presence of a low chloride level obviously other retained anions inorganic or organic are preventing the expected reciprocal expansion of bicarbonate The normal close relationship and predictability of the serum sodium concentration from the sum of serum bicarbonate and chloride in milliequivalents can be severely disturbed in renal impairment just as in diabetic ketosis therefore it becomes im-

*pendent on the urine volume, hence on the fluid intake of the patient* This is true even of normal subjects because of the limit to renal tubular concentration of urea, the chief urinary nitrogenous constituent Therefore a normal individual on a high protein intake but a relatively low fluid intake and with a low urine volume will show blood urea values several times the normal in the same range as a chronic nephritic with considerable renal impairment but on a normal or subnormal protein intake The kidney is quite flexible in its functional capacity but has very definite limits in some respects The correct interpretation of the simple test—the blood NPN or blood urea concentration—requires some knowledge of the preceding factors to prevent serious errors in diagnosis and treatment

Since the non protein nitrogen of the blood consists of several known and many unknown substances of different metabolic origin and behavior in the body especially in the kidney, it is more profitable to deal with the individual constituents of this melange Urea uric acid creatinine *creatine a host of amino acids, ammonia glutathione* and other small polypeptides are involved but from the practical standpoint of renal insufficiency the first three substances are of primary interest *Urea* reflects catabolism of both exogenous and endogenous protein *uric acid* and *creatinine* especially the latter, are chiefly the end stage of endogenous or tissue protein wear and tear Hence urea excretion will be much more variable also its retention There are other significant differences All are filtered by the glomeruli but urea diffuses back in the tubules so that only from 30 to 70 per cent of the filtered amount appears in the final urine *Creatinine* once filtered does not go back into the renal blood for this reason it is an excellent measure of the glomerular filtration rate at ordinary endogenous blood levels It is, therefore not increased in the blood like urea when the patient happens to eat more protein than the average or drink less fluid On the other hand blood creatinine properly measured will accurately reflect decreases or increases in glomerular filtration regardless of the urine volume at the time Urea may be washed out of the body by forcing fluids and its formation sharply reduced by a diet high in carbohydrate but low in protein or by parenteral glucose, which produces normal blood levels even with considerable renal impairment At such times the blood creatinine will still be elevated and furnish a true index of the state of renal function Hence its great prognostic significance when a concentration of 4 or 5 times the normal value has been reached This means very severe reduction in glomerular filtration, pre uremic because presumably tubular impairment and other damage is also extensive at this stage *Uric acid* is filtered and about 90 per cent reabsorbed It accumulates readily with reduction in filtration but unfortunately its blood level is subject to many other influences such as blood cell and other cellular breakdown and hormonal changes during infection toxemia various stresses, and metabolic disturbances The simple blood uric acid level *per se* cannot therefore, be used as a reliable indicator of renal function

When the blood urea and creatinine concentrations are elevated proportionally one is primarily dealing with the effects of renal insufficiency, when the blood urea is elevated out of all proportion to the creatinine level the state of renal function is not so bad as it seems from the urea value (very likely extrarenal factors are largely responsible) when the blood creatinine is elevated relatively *higher than the blood urea* the patient is suffering not only from renal insufficiency but from the effects of protein depletion and artificial (glucose) reduction in protein catabolism (aided by diuretic washing out of urea)

*Retention of inorganic electrolytes* also occurs in renal insufficiency Here, too one must consider individual solutes because of their varying origin in the body their interrelationships in body fluids and the selective response of the renal tubules to changes in the blood levels or the amount filtered by the glomeruli As Fishberg has pointed out one would not expect increased retention during renal insufficiency of any substance which the kidney normally retains or reabsorbs almost 100 per cent from the glomerular filtrate Therefore the blood *sodium* concentration does not rise as long as the normal complement of water can be reabsorbed with it On the contrary the effects of tubular damage and acidosis are often expressed by an increased urinary loss of sodium and a diminished serum level Retention of water may dilute the sodium in the body fluids The *sulfate* ion ingested or released in the body is normally almost entirely excreted *i e* filtered and not reabsorbed just like creatinine Therefore like creatinine it will be retained and to considerable levels in the blood when glomerular filtration is impaired and the exogenous supply continues in food drugs etc The significance of this retention lies in the fact that sulfate is an acid ion displacing the weaker carbonic acid or bicarbonate ion from its sodium partner and thus contributing to renal metabolic acidosis in the late

depression of bone marrow and a somewhat increased hemolysis. This anemia does not respond to any known therapy and hence requires repeated transfusions of blood.

*Etiology.*—The early restriction of the concept of uremia to the maximal renal insufficiency of acute or chronic organic renal disease is no longer tenable. The close interdependence of renal function and circulatory dynamics, the peculiar response of renal dynamics to sudden or subacute depletion of extracellular fluids, the conversion of too prolonged functional or prerenal insufficiency into hypoxic anatomical tubular damage with clearly organic changes as the basis of the continuing uremia, and the almost entire analogy between the clinical and chemical features of so-called true uremia of organic origin and the advanced prerenal or extrarenal azotemias warrant combining the end results of all these types of renal insufficiency into the all-inclusive concept of uremia. However, the patient with functional uremia will present clinical findings of both the uremic syndrome and the precipitating underlying disease or dysfunction (*see* Page 1004). Furthermore, the treatment of uremia will naturally vary with the etiology of the renal insufficiency, but realization of the unity of renal and prerenal factors in uremia will help the physician prevent the onset of innumerable instances of prerenal azotemia and, at the same time, find the remediable prerenal factors in uremias of organic origin. For the best interests of the patients, uremia is indivisible but of multiple etiology and with multiple metabolic disturbances capable of responding to selective therapy.

*Symptoms.*—The symptoms of uremia are as varied as its origins and chemical signs and involve every system of the body. Typically, the patient with chronic renal disease at the uremic stage complains of severe anorexia and nausea and may vomit on any attempt to take food or drink. He also complains of intolerable pruritus and dryness of the skin, general restlessness, irritability, and involuntary movements of the limb muscles. Furthermore, he is subject to headache, dizziness, ringing in the ears, insomnia or unusual drowsiness, overpowering weakness and exhaustion, and heavy breathing on the slightest exertion or even at rest. He finds his mouth and throat dry. Often he has a hacking nonproductive cough, palpitation and a sense of oppression in the chest, which may change into severe precordial pain with varying radiation to shoulders and arms upon the onset of uremic pericarditis. He is conscious of vague abdominal discomfort or of actual cramps. These pains are associated with diarrhea; the stools may be streaked with blood or may be tarry. Disturbed vision, transitory or permanent; sudden temporary weakness of the limbs, difficulty in speech, and confusion as to time and place are other symptoms manifested in uremia.

The patient may first be seen in a state of semi-stupor, stupor or deep coma, the pupils contracted and the breathing deep and acidotic (Kussmaul type). Occasionally the patient may be found, his eyes rolled up, in a convulsion with opisthotonus, tonic and clonic movements and involuntary urination. Often he is found in a state of complete mental disorientation with restlessness and violent activity requiring restraint or heavy sedation.

The signs of uncomplicated uremia include brownish yellow pallor, malnutrition, wide stare, prominent eyeballs (without true exophthalmos), scratch marks and a variety of rashes (often drug induced), dehydration or edema or both (in different regions), bleeding from the nose or gums, purpuric spots (especially on the lower extremities), coarse muscular twitching or tremors along with reflex hyperirritability and muscle weakness, and occasionally tetanic spasms or positive Chvostek and Trousseau signs. There may be pulmonary rales or signs of free pleural fluid. The cardiac findings will vary with the associated condition, such as prolonged hypertension. A localized or widespread pericardial friction rub may be heard. Gallop rhythm and hemic or other murmurs are common. Kussmaul, Cheyne-Stokes or stertorous respiration may be present. Venous collapse or venous engorgement may occur depending on associated conditions and the state of hydration. The pulse rate and volume will vary with the state of the circulatory system, but relative bradycardia is not un-

perative to analyze for sodium directly if restoration of body fluid electrolytes is to be made accurately and safely

Retention of *organic acids* occurs in renal insufficiency usually as the result of starvation or complicating diabetic ketosis in which condition the ingestion or production of these acids exceeds the capacity of the body to metabolize them and the ability of the impaired kidney to excrete the excess In the absence of direct analyses for individual or total organic acids the presence of such acids in increased amount can be deduced from the discrepancy between the total base concentration of the serum or more simply the sodium figure and the sum of the determined inorganic anions or acids namely bicarbonate, chloride phosphate and sulfate and protein Ketones and lactate usually form the chief organic acids small amounts of possibly toxic aromatic acids are also retained

*Acidosis* of the metabolic type is common in severe renal insufficiency It should be added that the loss of tubular ability to secrete ammonia is an important factor in the development of renal acidosis the reduced filtration of acids by the diseased glomeruli is aggravated by the increased tubular loss of sodium and other bases through lack of ammonia production which normally tends to spare fixed base from excretion The administration of any acid-forming salts like ammonium chloride becomes a dangerous procedure under these circumstances In fact the poor response of the impaired kidney to changes in acid base balance renders the development of either metabolic acidosis or alkalosis very easy in the pre terminal and terminal stages of chronic renal disease or in the acute toxic nephroses

*Retention of water* is also possible as a result of pure renal insufficiency whether acute or chronic Although dehydration for the usual reasons is very common in renal failure retention may occur whenever the intake of fluids exceeds the outgo in the urine sweat, or gastrointestinal losses Normally however this is virtually impossible because the kidneys can excrete from 25 to 30 liters of water a day if they are forced to, as in diabetes insipidus But in severe renal disease or functional impairment the reduced glomerular filtration of water and the back-diffusion of filtered water through damaged proximal or distal tubules conspire to limit sharply the excretion of water by the kidney The daily figure may be three liters a few hundred cubic centimeters or zero (anuria) The so called polyuria of renal insufficiency is rarely more than from 10 to 15 per cent of the capacity of true polyuria by normal kidneys The retention of water on a purely renal basis is possible and edema results Its electrolyte composition may be extremely abnormal because of the loss of tubular selectivity for ions at this stage The dangers of this situation are preventable by proper management of the afflicted subject s intake of water and electrolytes This is lifesaving in acute toxic or obstructive anurias

## UREMIA

Uremia is the culmination of the metabolic disturbances resulting from complete renal decompensation whether this is a matter of days or of decades In either case the final clinical picture is the same

Essentially uremia is a clinical syndrome resulting from *severe renal insufficiency due to organic or functional causes* and embracing the whole array of fluid and electrolyte disturbances non protein nitrogen retention acidosis and other metabolic disintegration But uremia according to many competent observers is also a *toxemia* although the nature of the toxin is unknown

A number of substances from organic metabolites like guanidine derivatives to free phenols and other aromatic products of protein break down in the gastrointestinal lumen or tissue cells have been held responsible for this toxin In addition there has been a convincing array of experimental work connected with renal hypertension and its mechanisms to point toward the noxious role of renal autolytic products in the origin of vascular necrosis and other lesions in uremic animals The entire problem of the function of the kidney as a source of pressor substances on the one hand and of a normal anti pressor mechanism on the other is involved in these studies Suffice it to say that correction of the usual body fluid and electrolyte disturbances in renal insufficiency do not dispose of the under lying general metabolic derangement for which it is logical to assume that retention of some toxic substances of extrarenal (or possibly renal) origin is responsible One of the obvious major effects of the hypothetical toxemia is the *anemia of renal insufficiency* which has so far defied close analysis but is apparently compounded of

the nature of the etiological process in the kidney or elsewhere (examples are the leucine and tyrosine crystals in acute yellow atrophy of the liver and the hemoglobin derivative casts in hemolytic transfusion reactions) In chronic Bright's disease with uremia the urinary sediment may contain the very wide waxy or granular 'renal-failure' casts described by Addis as pathognomonic In the absence of a hemolytic syndrome phenolic poisoning or porphyria the urine in uremia is usually light in color for the normal urinary pigments or their precursors are seldom excreted in adequate concentration The dilute urines of uremia become more ominous when the daily volume drops to a pint or less as is often the case Casts and cells dissolve readily in these dilute hypotonic urines and this tends to make qualitative or differential diagnosis difficult Bacteriological culture may reveal infection of the urinary tract and show the kind of infection but will not alone of course point out the site of infection Chemical analysis of the 24-hour urine for sodium potassium and chloride excretion may be valuable in determining the degree of electrolyte loss and type of replacement therapy indicated Unusual urinary calcium excretion (Sulkowitch test) may point to hyperparathyroidism or vitamin D overdosage as a possible basis for uremia The finding of Bence-Jones protein in the urine of a uremic is also of considerable diagnostic value

*Treatment* —The treatment of uremia depends on the cause of the renal dysfunction Much can be done to prevent uremia especially functional uremia rapid correction of shock dehydration and electrolyte depletion usually forestalls severe renal insufficiency This requires accurate observation of the patient for signs of circulatory impairment complete measurement and recording of all urine vomitus aspirated gastrointestinal fluid and diarrheal stools with due allowance for profuse sweating and increased insensible perspiration associated with fever and dyspnea accurate tally of all fluid and electrolyte administered including blood and plasma frequent chemical analyses for serum sodium chloride bicarbonate potassium and blood NPN or urea and creatinine The proper management of diabetic ketosis or of Addison's disease in crisis requires no argument The prevention of uremia in all these conditions is largely a matter of good bookkeeping knowing accurately the intake and output of fluid and electrolytes and of maintenance of well-oxygenated circulating volume under adequate blood pressure

Prevention of uremia in severe acute glomerulonephritis and in the acute toxic nephroses including the so-called lower nephron nephrosis is essentially based on sharp restriction of dietary protein to 20 grams or less a day exclusion of salt from the diet and limitation of the potassium intake Carbohydrate and fat provide the necessary calories Up to 300 grams of glucose may be given intravenously in concentrated form if the patient is unable to retain food Treatment of actual or impending cardiac failure by the appropriate measures (except for the use of mercurials or purine diuretics) the use of BAL (dimercaptopropanol) early in mercurial nephrosis the interruption of sulfa or other drug therapy possibly responsible for the renal damage the administration of penicillin aureomycin or other antibiotics as indicated to control an underlying infection or prevent pulmonary infection in previously edematous lungs or bladder infection in catheterized patients—all these are also necessary measures for the prevention of uremia It is exceedingly important to prevent hypertensive encephalopathy or any other strain on the circulation In any case with oliguria involving the slightest doubt as to etiology the possibility of urinary-tract obstruction by calculus should be excluded by *x* ray films and if necessary by cystoscopy and retrograde urography

In older patients with congestive heart failure or hypertensive disease uremia may result from excessive sodium and chloride depletion by mercurials and rigid low sodium diets This low sodium syndrome is characterized by low serum sodium values (chloride may be normal if ammonium chloride is being given) and elevated blood-urea levels along with many of the symptoms found in early uremia Prevention of this syndrome often fatal if not recognized

usual except during acute heart failure The abdomen may be scaphoid or distended and moderately tender over the bowel The kidneys may be unpalpable or enlarged and tender Ascites may be present when there is general edema The extremities are often wasted from inactivity and weight loss and may or may not be edematous Muscle hyperesthesia is common Reflex clonus and other abnormal reflexes may be elicited Stomatitis ulcerative pharyngitis *suppurative parotitis and regional lymphadenitis* are less frequently seen in these days *of better oral hygiene*

To the above description must be added the *signs due to hypertensive vascular disease,* acute or chronic, often associated with the renal disease that results in uremia In acute glomerulonephritis or eclamptic toxemia uremia is associated with elevated systolic and diastolic blood pressure hard wiry pulse and the following eye signs narrow or irregularly constricted retinal arterioles and flame-shaped hemorrhages, cotton-wool exudates and varying degrees of papilledema or choking of the disc Other associated signs are accentuated heart tones and possibly dilatation along with the episodic findings of acute left ventricular failure or pulmonary edema or of general heart failure with venous engorgement, hepatic enlargement and tenderness In the chronic hypertensive patient evidence of cardiac hypertrophy and enlargement aortic sclerosis and dilatation retinal arteriolosclerosis and varying degrees of retinopathy and signs *of organic changes in the* central nervous system as a result of vascular *disease or accident* will be superimposed and intermingled with the syndrome of uremia to produce a complex and unhappy clinical picture

In the *functional uremias* which arise from circulatory, hemorrhagic or traumatic shock, severe infectious diseases acute dehydration from gastro intestinal obstruction aspiration by drainage tubes and a great variety of other conditions reflecting themselves in severe renal impairment the symptoms and signs of the original disease vascular accident or disturbance will be inextricably interwoven with the *symptoms* and signs of uremia *per se*

The diagnosis of uremia the *laboratory findings* must include proof of non protein nitrogen retention in the blood and evidence of impaired urinary excretion or impaired concentrating ability on the part of the kidney Some electrolyte change is almost always apparent In general uremia is usually associated with blood NPN values of 75 mg per cent or higher and with blood urea nitrogen figures of 50 mg per cent or higher The blood creatinine may be relatively less elevated or proportionately increased, depending on the cause and duration of uremia but it is never *normal as in* the azotemias unrelated to renal impairment *Until there is some specific test for a specific* uremic toxin the chemical diagnosis of *uremia* will be tricky *if taken alone The* diazo reaction for uremia and tests for indican or free *phenols are reasonably* reliable in cases of chronic uremia but are often negative in cases of acute uremia No reliance can be placed on serum-electrolyte estimations in diagnosing uremia Acidosis or alkalosis may be found, the former the more commonly However elevations of serum inorganic phosphate and sulfate when present together are a highly significant indicator of chemical uremia Electrocardiographic changes in uremia will reflect cardiac muscle hypertrophy or damage calcium or potassium disturbances pericarditis or the effects of cardiac drugs

The *urine* in uremia is characterized by relatively *fixed specific gravity* from 1 010 to 1 016 or isosthenuria due to loss of tubular concentrating *power for urea* which in spite of high blood levels may not be eliminated *at a greater rate* than that indicated by even a low daily production Urea excretion at this stage depends almost entirely on urine volume other things being equal The urine is also only weakly acid rarely less than pH 6 and contains almost no ammonia (unless there is heavy bacterial contamination of the urinary passages or the urine container) There is very little titratable acidity a reflection of *decreased* glomerular filtration of phosphates and of distal tubular *inability to convert* alkaline disodium to acid dihydrogen phosphate *There is always proteinuria* of varying degree and the urinary sediment may reflect

the nature of the etiological process in the kidney or elsewhere (examples are the leucine and tyrosine crystals in acute yellow atrophy of the liver and the hemoglobin derivative casts in hemolytic transfusion reactions) In chronic Bright's disease with uremia the urinary sediment may contain the very wide waxy or granular renal failure casts described by Addis as pathognomonic In the absence of a hemolytic syndrome phenolic poisoning or porphyria *the urine in uremia is usually light in color* for the normal urinary pigments or their precursors are seldom excreted in adequate concentration The dilute urines of uremia become more ominous when the daily volume drops to a pint or less as is often the case Casts and cells dissolve readily in these dilute hypotonic urines and this tends to make qualitative or differential diagnosis difficult Bacteriological culture may reveal infection of the urinary tract and show the kind of infection but will not alone of course point out the site of infection Chemical analysis of the 24 hour urine for sodium potassium and chloride excretion may be valuable *in determining the degree of electrolyte* loss and type of replacement therapy indicated Unusual urinary calcium excretion (Sulkowitch test) may point to hyperparathyroidism or vitamin D overdosage as a possible basis for uremia The finding of Bence-Jones protein in the urine of a uremic is also of considerable diagnostic value

*Treatment* —The treatment of uremia depends on the cause of the renal dysfunction Much can be done to prevent uremia especially functional uremia rapid correction of shock dehydration and electrolyte depletion usually forestalls severe renal in*sufficiency* *This requires accurate observation* of the patient for signs of circulatory impairment complete measurement and recording of all urine vomitus aspirated gastrointestinal fluid and diarrheal stools with due allowance for profuse sweating and increased insensible perspiration associated with fever and dyspnea accurate tally of all fluid and electrolyte administered including blood and plasma frequent chemical analyses for serum sodium chloride bicarbonate potassium and blood NPN or urea and creatinine The proper management of diabetic ketosis or of Addison's disease in crisis requires no argument The prevention of uremia in all these conditions is largely a matter of good bookkeeping knowing accurately the intake and output of fluid and electrolytes and of maintenance of well-oxygenated circulating volume under adequate blood pressure

Prevention of uremia in severe acute glomerulonephritis and in the acute toxic *nephroses including the so-called lower* nephron nephrosis is essentially based on sharp restriction of dietary protein to 20 grams or less a day exclusion of salt from the diet and limitation of the potassium intake Carbohydrate and fat provide the necessary calories Up to 300 grams of glucose may be given intravenously in concentrated form if the patient is unable to retain food Treatment of actual or impending cardiac failure by the appropriate measures (except for the use of mercurials or purine diuretics) the use of BAL (dimercaptopropanol) early in mercurial nephrosis the interruption of sulfa or other drug *therapy possibly responsible for the renal* damage the administration of penicillin aureomycin or other antibiotics as indicated to control an underlying infection or prevent pulmonary infection in previously edematous lungs or bladder infection in catheterized patients—all these are also necessary measures for the prevention of uremia It is exceedingly important to prevent hypertensive encephalopathy or any other strain on the circulation In any case with oliguria involving the slightest doubt as to etiology the possibility of urinary tract obstruction by calculus should be excluded by *x* ray films and if necessary by cystoscopy and retrograde urography

In older patients with congestive heart failure or hypertensive disease uremia may result from excessive sodium and chloride depletion by mercurials and rigid low-sodium diets This low-sodium syndrome is characterized by low serum sodium values (chloride may be normal if ammonium chloride is being given) and elevated blood-urea levels along with many of the symptoms found in early uremia Prevention of this syndrome often fatal if not recognized

early, depends on discovery of serum-electrolyte losses and replacement of these losses. Only half the necessary replacement in sodium and chloride should be administered at first and the patient's reaction, *his urine and serum-electrolyte changes* should be carefully observed. Usually, a hypertonic solution is indicated in the presence of edema to avoid overdilution of the *injected electrolyte*.

The prevention of uremia in chronic bilateral renal disease with severe functional impairment or in the pre-uremic state is based on a diet low in protein—from 30 to 50 grams of protein daily. The diet must provide enough calories to spare body protein and must provide a fluid intake of at least 3 liters a day to assure a urine volume of from 1500 to 2000 cc. and delay accumulation of non-protein nitrogen. The dietary salt intake must be restricted if edema is present. A very dilute urine like a very concentrated urine means extra work for the tubules, hence salt may be useful *when the urine is not adequately concentrated*. If the patient develops anorexia or *vomiting, parenteral fluids must be given early*. The use of acid-forming salts, alkali in large doses, mercurials or sedatives dependent on the kidneys for excretion should be avoided in the pre-uremic stage because of their harmful effects. Circulatory failure must be carefully guarded against in chronic renal disease. Acidosis must be looked for and treated with the required amounts of sodium bicarbonate or sodium citrate orally or sodium bicarbonate or sodium lactate intravenously.

The *management of uremia* is essentially *symptomatic*. *Anorexia, nausea and vomiting* usually do not yield to bland foods and small meals but often require parenteral feeding for a few days at a time to allay gastric irritability. The amount of fluid given, the type of electrolyte mixture, the use of amino acids, plasma or serum albumin, the concentration of glucose—all these will be determined by the patient's needs, the urinary output, and the serum analyses. In giving saline solutions the chloride should be diluted by the addition of sodium lactate or bicarbonate in order to maintain the 3:2 ratio of *sodium to chloride* in the normal serum. Whenever intravenous alimentation is necessary, adequate amounts of the vitamin B group and ascorbic acid should be given daily in the infusion fluid. The patient's bowel movement should be encouraged by small enemas; profuse colonic irrigations *should be avoided*. Anemia, if the hemoglobin falls below 60 or 70 per cent, may be temporarily corrected by transfusion of perfectly typed and cross-matched packed *red cells*. *No more than 250 cc. should be* given at any one time; this is easier on the patient's vascular system than 500 cc. of whole blood and furnishes the same amount of oxygen carriers.

*If the patient is oliguric and does not increase his urine volume on receiving fluids* but, instead, develops edema, there is no point to forcing more fluid into his body; only pulmonary edema, general anasarca or convulsions will result.

Adequate sedation is indicated to prevent or allay pain, nausea, respiratory difficulty, restlessness, anxiety, fear, insomnia, pruritus, twitching or convulsion. A low serum calcium is *corrected with calcium* salts given parenterally. In hypertensive *encephalopathy, careful spinal tap* and relief of pressure may be of value. Some patients soon require large and frequent doses of sedatives or hypnotics. There is no reason for withholding them if they make the patient's terminal period more tolerable. Unfortunately, many uremic individuals retain consciousness and capacity for suffering long after any prospect of even temporary remission has vanished.

The use of peritoneal or intestinal irrigation in the treatment of acute anuric uremia due to reversible renal disease has not strikingly reduced the high mortality rate. The artificial kidney or dialyzing apparatus of various types carries more promise but is still a formidable procedure because of problems of hemolysis, electrolyte and fluid balance, technical skill and other factors. However, there is reason to be optimistic about the future development of such mechanical devices.

## RENAL OSTEODYSTROPHY

This designation covers all disturbances in bone morphology resulting from osteoporosis associated with renal insufficiency. It may

be found in patients with primary renal disease (acquired or congenital organic or functional tubular) or with renal disease secondary to primary endocrine or metabolic *disturbances or to obstructive lesions in the* urinary tract. The bony changes include decalcification, loss of matrix, osteitis fibrosa and cystic changes, with pseudo fractures and deformities. Children are more strikingly affected because of the unique requirements of growing bones. The demineralization is produced in organic renal insufficiency by retention of inorganic phosphate and urinary loss of calcium in the acidosis due to impairment of renal production of ammonia. It may be aggravated by deficient dietary intake of calcium or poor absorption from the gastrointestinal tract. On the other hand, rachitic demineralization of bones may result from functional impairment of tubular reabsorption of phosphate as in the Fanconi syndrome of children or certain types of adult osteomalacia. Primary hyperparathyroidism acts early to promote renal loss of phosphate and calcium and at the same time mobilizes these substances from bone. In later stages secondary renal disease and renal insufficiency add to the pathological physiology. The degree of bone involvement in renal insufficiency is also determined by the response of the parathyroid glands to hyperphosphatemia and hypocalcemia. Over compensation may result in hypercalcemia and its consequences and in bone dystrophy of extensive degree.

*The symptoms* will depend on the duration and degree of the osteodystrophy. In children the clinical picture may be one of resistant rickets, as in the Fanconi syndrome and the group with hyperchloremic nephrocalcinosis described by Albright *et al.* The deformities of knees, ankles and wrists *originally described as due to renal rickets* and often associated with impaired growth are observed in adolescent children with advanced chronic glomerulonephritis or pyelonephritis, with polycystic kidneys or with congenital dilatation of the ureters and renal pelves and marked renal atrophy. In adults, skeletal pains or fractures may lead to *x* ray examination of the bones and disclosure of the osteoporosis and other changes even before renal insufficiency is suspected. In many uremic individuals the osteoclastic involvement of bone is revealed only at autopsy when systematic *examination is stimulated by the finding of* hyperplastic or adenomatous parathyroid glands.

*Treatment* of renal osteodystrophy will vary with the underlying disease. The treatment can be *preventive* to the extent that renal insufficiency and acidosis can be counteracted. When ammonia formation is inadequate, sodium citrate or bicarbonate is given daily in amounts sufficient to correct hyperchloremic acidosis and maintain normal serum sodium levels. Hypophosphatemia in the Fanconi syndrome is treated with dietary supplements of phosphate and extra vitamin D. Hyperphosphatemia in renal insufficiency may be reduced by diet high in calcium, low in phosphate and by *administration of large doses of aluminum* hydroxide gel to prevent absorption of phosphate. In children vitamin D in doses up to 5000 or 10 000 units daily may help to elevate the serum calcium to normal levels. Dihydrotachysterol (AT-10) may be more effective in some cases. Hyperparathyroidism, if primary, is dealt with surgically; secondary hyperparathyroidism can be treated only by management of renal insufficiency and phosphate retention.

## PATHOLOGY OF RENAL DISEASES

The pathology of diseases of the kidneys is a large subject in itself and will be discussed only insofar as it throws light on the classification and pathological physiology of renal diseases. Certain conditions, such as embolic infarction of the kidney, neoplasms and cystic transformation, hemorrhages in the parenchyma in scurvy, hemophilia or various purpuras and lymphomas, hydronephrosis or pyonephrosis due to obstruction of pelvis or ureter, focal scarring due to old inflammatory or vascular atrophy of tissue and replacement fibrosis, toxic necrosis, nephrolithiasis of various types, caseating tuberculosis or pyogenic suppuration—these and other gross conditions can be readily diagnosed on inspection after a little experience and correlated with the clinical data on

the patient However, recognition of certain forms or stages of chronic glomerulonephritis, amyloidosis, diabetic glomerulosclerosis even chronic pyelonephritis and hypertensive nephrosclerosis may be difficult from the gross description alone of the enlarged or reduced kidneys, the nature of the cortical markings the apparent amount of fat or other infiltrate, the smoothness or granularity of the surface and the coloration Histologic sections must be depended upon for differential diagnosis especially in the older age groups in which vascular disease may be superimposed on the basic renal pathology Even after studying the microscopic slides an estimate as to renal function during life may be highly hazardous in view of the role of hemodynamic factors not

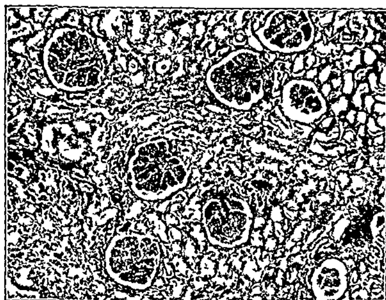


FIG 160 —Acute proliferative glomerulonephritis Note large cellular glomeruli and normal tubules Photomicrograph low magnification (Bell s Renal Diseases )



FIG 161 —Severe acute hemorrhagic glomerulonephritis from a case of bacteremia* The capsular spaces and tubules are filled with erythrocytes Photomicrograph (Bell s Renal Diseases )

registered in the kidney sections. The relative degrees of glomerular and tubular damage are even more difficult to assess anatomically unless one studies numerous nephrons teased out in their entirety by the ingenious technique of Oliver. In view of these difficulties it becomes unreasonable for either the clinician or the pathologist to expect a close correlation between functional and anatomical changes. However it is not at all unwarranted for both to expect that a fairly accurate diagnosis should be possible from an adequate clinical history, physical and laboratory findings, and an opportunity to observe carefully at least a part of the course of the disease. The reason for this is that the various diffuse diseases of the kidneys do have an individual life

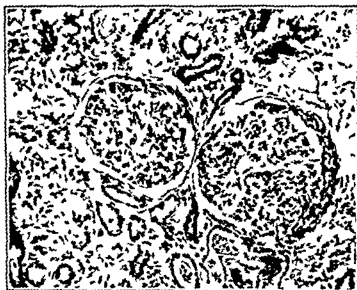


Fig. 162.—Subacute glomerulonephritis. Nearly all the glomerular capillaries are completely closed and there is severe diffuse tubular atrophy. Photomicrograph. (Bell's Renal Diseases.)

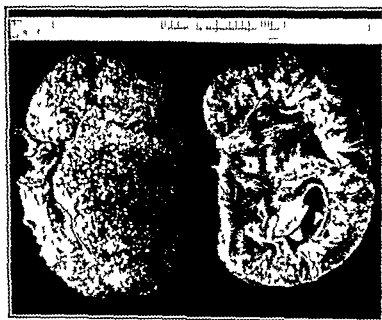


Fig. 163.—Chronic azotemic glomerulonephritis. Contracted kidney. (Bell's Renal Diseases.)

history or biologic course, even though there may be considerable overlapping in symptoms signs and pathological findings The overlapping is often due to hypertension which may initiate a whole evolution of functional and organic cardiovascular abnormalities

One serious defect of pathological material obtained from cases of chronic renal diseases is that it usually represents the last stages of the disease (uremia)

On the other hand accidental disclosure after death from some other cause, of early renal lesions in individuals not suspected of having kidney disease is of relatively little value in correlation studies The actual histology of mild acute glomerulonephritis that ends in recovery, of moderate nephritis that lasts for decades of recurrent acute pyelonephritis in its earlier attacks or the beginnings of glomerulosclerosis—these and other pathological renal phenomena are still much of a mystery to the pathologist because the material is unavailable for study, except by means of biopsies difficult to obtain This is a field worth developing like hepatic biopsies in recent years

## CLASSIFICATION OF RENAL DISEASES

The following classification of renal diseases is modified from the classical contributions of Bright Gull and Sutton Volhard and Fahr, Addis and Oliver Bell, Fishberg, and many others It differs from the earlier groupings however in including the functional renal diseases in addition to the organic types

### Classification

A Organic Renal Diseases

1 Glomerulonephritis, diffuse—acute chronic
2 Glomerulitis focal—toxic embolic thrombotic allergic
3 Glomerulosclerosis—arteriolar (hypertensive) diabetic
4 Glomerulonephrosis—amyloid lipoid pregnancy
5 Pyelonephritis—acute chronic
6 Vascular—arterio arteriolosclerotic (hypertensive) occlusive allergic toxic
7 Tubular nephroses (necrotizing)—toxic, hemodynamic, endocrine or metabolic, hemolytic obstructive
8 Congenital malformations—polycystic kidneys
9 Nephrolithiasis
10 Neoplasms—benign malignant

B Functional Renal Diseases

1 Glomerular arteriolar constriction—proteinuria hypertension cardiac failure constrictive pericarditis toxemia of pregnancy early shock
2 Tubulovascular syndrome—severe shock acute tubular hypoxia of other origin
3 Tubular hormonal—diabetes insipidus adrenal cortical disease or dysfunction, hypertension(?), adaptation to stress parathyroid disease pregnancy
4 Tubular, enzymatic—renal diabetes Fanconi syndrome dietary effects hypertension(?) drug effects
5 Venous congestion—postural proteinuria, cardiac failure

## DIAGNOSIS IN RENAL DISEASES

Diagnosis in renal diseases is based on a knowledge of the natural history of each disease, of the pathological process in the kidneys of the pathological physiology and the resulting symptoms and signs and the urinary changes characteristic of some renal diseases

*The Urine* —The urine reflects the pathological renal process provided the products of renal inflammation or degeneration have access to the urine Completely scarred glomeruli and obliterated tubules cannot affect the urine nor can interstitial inflammation if tubular walls have not been broken through by the cellular infiltrates or bacteria On the other hand since the urine has to pass through the postrenal urinary tract before it reaches the centrifuge tube and the microscope, it may pick up evidence of disease or irritation anywhere along the way including material from the prostate, epididymis seminal vesicle uterus and vagina In many cases the history will disclose symptoms clearly referable to the lower urinary tract and aid the examiner in interpretation of the urine or in the decision to obtain specimens by catheterization of the bladder particularly in the female Other important aids include the technique of collecting urine in 2 or 3 containers during a single voiding, to determine the urethral or bladder origin of pus shreds or gross blood voiding of urine before and after prostatic or seminal vesicular massage and cystoscopic examination ureteral catheterization and x ray contrast studies

The *gross appearance* of the urine may be diagnostic for example of hematuria hemoglobin

uria (or methemoglobinuria) porphyrinuria melanuria alkaptonuria bilirubinuria certain drugs and dyes in the urine uric acid and urates pyuria and other abnormalities In other instances careful chemical tests may be necessary

For *microscopic study* the freshly voided urine is the best specimen to examine unless it is dilute or alkaline Formed elements rapidly dissolve in such urine and even proteinuria may fail of detection unless very careful acidification is carried out Ideally the best urine to examine is that obtained under conditions of dehydration as in the Addis concentration test This means having the patient eat the normal solid articles of diet—meat potatoes bread butter cream eggs cheese cereals desserts sugar salt etc—but avoid all liquids 5 or 10 per cent carbohydrate vegetables and juicy fruits for 18 hours If an Addis count is to be made on the urinary sediment the 12 hour urine (from 9 P M to 9 A M ) is collected in one container However if the patient voids before retiring and saves the urine passed on arising in the morning it will be satisfactory for qualitative examination This urine should have a maximum specific gravity be strongly acid and contain formed elements in a good state of preservation Centrifugation at a low or moderate speed for a few minutes will produce a good sediment sufficient for diagnostic purposes without the need for an accurate Addis count which requires a fair amount of technical experience The important thing is that the physician obtain a urine as though for an Addis count and then examine the sediment himself He will be rewarded by a wealth of findings in urines from patients with renal disease Absence of red cells leukocytes and casts in a highly concentrated (above 1 026) acid urine, properly centrifuged and prepared for microscopic study is strong evidence against active renal disease Satisfaction with negative reports on urines of variable reaction and of specific gravities ranging from 1 010 to 1 018 or so is risky especially in the presence of proteinuria or of a recent history of abnormal urines

*Proteinuria* by the usual clinical tests may be present in traces in normal urines containing secretions from the accessory sex glands in the male or female The amount of protein in urine is helpful in differentiating renal disease from disease of the lower urinary tract In the former much more protein is found relative to the number of leukocytes or red blood cells in the sediment This is understandable in view of the larger amount of protein that may leak out through the millions of damaged glomeruli in diffuse renal disease In inflammations of the lower urinary tract the proteinuria is derived from a relatively small amount of exudate diluted by the entire urine volume However this is only a relative distinction and does not help much in diagnosing diffuse diseases of the kidney in stages with little proteinuria for one reason or another In judging the quantitative significance of proteinuria the concentration of the particular urine specimen must be taken into account This is often neglected in conclusions from changes in the number of plusses or grades of proteinuria on different occasions Quantitative analysis for protein in a 12 hour or 24 hour urine collection is essential in all patients with considerable proteinuria or lowered serum protein values in order to determine the need for extra protein in the diet However a marked proteinuria may diminish sharply in patients on a low protein intake

It may be useful in certain cases to test the urine specifically for *serum globulins* as an index of the severity of the renal pathology especially in glomerulonephritis and amyloidosis Ordinarily the urinary protein consists of about 90 per cent serum albumin and only small amounts of the globulin fractions The percentage of globulin has been reported to be much higher in the more severe types of glomerulonephritis as confirmed by autopsy observations The specific *Bence-Jones proteins* in the urine of patients with multiple myeloma and other diffuse bone diseases are readily detected by their peculiar heat solubility It is good routine in any laboratory equipped with a 56 60 water bath to place in this bath all urines that show even slight clouding well before the boiling point as the heat and acetic acid test is carried out When the sulfosalicylic acid reagent is used in the cold specimen there is all the more reason for warming up the precipitated urine to 60 in order to detect Bence Jones proteins They are not infrequently associated with ordinary serum proteins in the urines of older patients with multiple myeloma

Proteinuria is only an indicator of renal dysfunction altered glomerular permeability or diminished tubular reabsorption of filtered protein It is therefore not limited to organic renal diseases but is in fact a frequent accompaniment of numerous infectious diseases toxemias circulatory failure allergic reactions and other disturbances affecting the general body economy Postural proteinuria is very common in children

*Hematuria* is perhaps the most important single urinary abnormality because it may be grossly visible to the layman and therefore immediately calls attention to the existence of urinary tract disease But it is also nonspecific to a large extent because any inflammation trauma congestion neoplasm ulceration calculus or gravel—from the kidney on down to the urinary meatus—may give rise to gross or microscopic hematuria To list the possible causes of hematuria is merely to list every disease of the urinary tract plus every systemic cause of hematuria such as all hematological disorders with disturbances in coagulation or capillary fragility vitamin C deficiency allergic reactions of bac

terial or drug origin and various types of toxemia and septicemia. However in chronic glomerulonephritis and renal vascular disease, hematuria is of great significance as a measure of the activity of the inflammatory process in the glomeruli or of acute vascular obliteration or allergic process.

*Hematuria*, almost always microscopic, is the chief criterion of the numerous varieties of glomerulitis and may lead to the first suspicion of the underlying general disease or toxemia. The characteristic of *glomerular hematuria* is that some of the red cells or their *breakdown pigments may be trapped in* casts as they pass down the renal tubules. This obviously cannot occur in the case of bleeding distal to the nephron and is therefore *of high diagnostic value in localizing the* source of the bleeding. *Red blood cell casts* often contain only the ghosts of erythrocytes. Erythrocytic ghosts are also found free in the urine and *in fresh concentrated acid* specimens suggest renal parenchymal origin, whereas normal looking hemoglobin filled red blood cells are more likely to derive from the lower urinary tract. The use of a catheter to obtain the specimen from the bladder, and especially the ureter, may give rise to slight traumatic microscopic hematuria. *The finding of a single authentic* red cell cast is of significance. In all cases, however, the urinary sediment if not grossly bloody should be tested for blood with the *guaiac or the benzidine reagent*.

*Cylindruria* or casts in the urine may be a valuable diagnostic and prognostic index. Casts are formed by precipitation of filtered *plasma protein in the distal and collecting* tubular lumen, aided by the pH, the chemical action of chondroitin sulfuric acid, the salting-out effect and other factors (Oliver). *In these hyaline or waxy casts, granules of* cytoplasmic protein extruded from degenerating tubular epithelium or granular conversion of desquamated renal cells become imbedded to form granular casts. Similarly epithelial casts arise from desquamated but still recognizable tubular epithelium. Erythrocytic casts have already been mentioned. *Leukocytic* or pus casts develop in pyelonephritis and at times in severe acute glomerulonephritis. Finally there are the refractile fatty casts containing renal epithelial cells *or granules with both neutral* isotropic fat and the *doubly refractile, or anisotropic, lipoids*. These last are of great diagnostic importance in differentiating chronic glomerulonephritis, amyloidosis and diabetic glomerulosclerosis, on the one hand, from the large group of cases of pyelonephritis and hypertensive or arteriosclerotic renal vascular disease on the other. This simple but valuable aid to diagnosis has not been sufficiently utilized in spite of many years of acquaintance with it, by experts in the field of renal diseases. Similar value attaches to the finding of free floating fatty cells in the urinary sediment. The presence of brownish red granular *pigment casts* should arouse the suspicion of glomerular bleeding or of the products of intravascular hemolysis and hemoglobinuria. Special stains for iron (Prussian blue reaction) may reveal hemosiderin in casts or epithelial cells in the sediment and aid in the diagnosis of pernicious anemia, hemochromatosis or hemosiderosis of various origin. In the absence of severe dehydration and sluggish urine flow due to acute febrile or metabolic diseases, wide casts of any variety usually spell uremia because they are found in cases of extensive parenchymal destruction. They form in the great ducts of Bellini at the very end of the collecting system (Oliver).

*Pyuria* is next to proteinuria the most common urinary abnormality. It usually indicates an active infection or *inflammation* in the urinary tract. It may occur as many individual leukocytes or leukocytes in clumps, masses or shreds of entangling mucus. *Pus casts are also seen when the* cells enter the urinary stream in the tubular lumen directly from interstitial infiltrates or from the glomeruli.

The less the proteinuria associated with pyuria, the more likely the lower urinary tract is the source of the leukocytes. Of course contamination with vaginal contents and prostatic or seminal vesicular secretion must be guarded against. When the urine is grossly cloudy and full of shreds, examination of the uncentrifuged sample is better as a measure of the amount of leukocytic component. The cells are in various stages of preservation and may be polymorphonuclear or mononuclear. They may show highly motile granules when specially stained (Sternheimer). The simultaneous presence of bacteria, bacillary or coccal, in the freshly voided specimen is strong evidence of infection as the basis of the pyuria.

The reaction of the urine and the ammonia content determined by urea-splitting organisms furnishes a clue to the type of bacteria involved. *Cultures* must be made to determine the nature of the microörganisms and to serve as a necessary guide for antibiotic therapy. The tubercle bacillus should always be remembered. The presence of pus in the urine requires the simple 2 or 3 glass test to determine the possible source in the anterior or posterior urethra. When this structure is excluded (and the glands draining into it) the problem is shifted to the bladder, ureters and renal pelves. The possibility of an obstructive lesion as the basis of secondary infection in the urinary tract is the first thought that should enter a physician's mind when he discovers pyuria in a patient with or without other symptoms. Much harm has been done by neglect of this simple fact.

*Crystalluria* may or may not be important. The sediment of many normal urines may contain crystals depending on the concentration, reaction, temperature and many other factors in the particular specimen. Thus a highly acid concentrated urine of a patient with fever and some dehydration may deposit a heavy mass of brick red urate crystals as it cools. Gentle warming may redissolve them. The alkaline urine of a nervous patient shortly after a meal may yield much triple phosphate material on centrifuging. Alkaline carbonates which effervesce on acidification and heating of the urine, oxalates that come down in nearly neutral urines, are common normally.

Whether a given sediment or repeated samples from the same patient contain an excess of uric acid, calcium-oxalate or calcium phosphate crystals, possibly related to the problem of urinary lithiasis or gravel, is usually very difficult to determine without other diagnostic information. On the other hand, various *sulfa* crystals in fresh urines, especially when associated with erythrocytes or their ghosts, may be of vital significance in assessing the danger of precipitation of these drugs in the urinary tract. Similarly, *cystine* crystals point to cystinosis and possible cystine lithiasis. The rare leucine and tyrosine crystals indicate severe hepatic damage. Bence-Jones protein and other interesting compounds may crystallize in the standing urine.

*Hemoglobinuria.*—Hemoglobin is found in the urine either as the result of secondary hemolysis after hematuria or as the direct effect of intravascular hemolysis and glomerular filtration of the free hemoglobin or other blood pigment derivatives.

While hemoglobin is reabsorbed by the normal renal tubule, the capacity is limited and the excess hemoglobin escapes into the urine, where it can be identified by the gross coloration and spectroscopic examination. Often pigment casts are present in the urinary sediment. The absence of hematuria is characteristic in true hemoglobinurias. Whenever hemoglobinuria is detected a sample of the patient's blood should be drawn under proper precautions for the determination of the presence of free hemoglobin in the serum. If the patient's hemoglobinuria is related to exposure to cold, prolonged exercise (march hemoglobinuria), nocturnal occurrence or allergy to fava beans (favism), specific induction of hemolysis may be the only way of proving the diagnosis.

Apart from its chemical and cellular content, the urine may furnish information by way of volume, diurnal distribution, frequency of expulsion and pain associated with the act. *Oliguria* and *anuria* have already been discussed (page 993).

*Dysuria.*—Dysuria or painful urination is often associated with frequent or urgent passage of urine. It may indicate inflammation, ulceration or congestion anywhere from the kidney to the external meatus. If occurring only at the beginning and end of urination, the seat of trouble is likely to be in the neck of the bladder. Continuous pain throughout urination speaks for urethral disease. Dysuria may be associated with renal or ureteral colic in urinary lithiasis or passage of blood clots. Prostatic hypertrophy in the male is a common cause of dysuria and frequency of urination. Cystitis and prolapse of the uterus in the female are very common. Dysuria brought on by bowel movement suggests prostatitis or seminal vesiculitis.

*Nocturia.*—Nocturia, apart from excessive intake of fluids during the evening or just before retiring, is an index of delayed renal excretion of water ingested or injected. This is most commonly the result of gross or occult cardiac failure, with latent edema developing during the hours of activity in the upright posture. With recumbency, excess fluid in the interstitial spaces re-enters the circulation and is made available to the kidneys. Furthermore, renal blood flow is increased during the recumbency and rest of the night hours, favoring increased urine formation. Nocturia may also be due to pri

mary renal impairment, usually advanced, with inability of remaining tubules to respond rapidly to diurnal changes in water content of the blood. Finally, nocturia may be post renal and associated with hydronephrosis or irritation of the bladder by infection, prostatic hypertrophy, diverticula, nervous system lesions or pressure by abdominal masses. In young children nocturia is likely to become enuresis. Though this is an expression of nervous tension and emotional conflicts, it also accompanies a variety of congenital anomalies and secondary inflammation or obstruction of the urinary tract.

Difficulty in starting the act of urination, incontinence of various degrees, changes in the caliber of the stream during its flow, intermittent stoppage with or without distress, retention for varying periods, splitting of the stream—all these are usually indicative of obstructive lesions in the bladder or urethra or of neurogenic disturbance in the motor function of the bladder and its sphincters. They require careful investigation of both the lower urinary tract and the patient as a whole.

## PROGNOSIS IN RENAL DISEASES

About 90 per cent of the children with acute glomerulonephritis completely recover but only 50 per cent of the adults with the disease recover. The severe hypertensive disease associated with unilateral atrophic pyelonephritis in the first 2 or 3 decades of life may be completely cured by nephrectomy, whereas in later years the same treatment usually fails. Early recognition of urinary tract obstruction and its surgical relief may put an end to recurrent attacks of pyelonephritis and progressive destruction of renal tissue. Antibiotics can have no more than a temporary effect on urinary tract infection in the presence of persistent obstruction.

The prognosis of uremia due to acute toxic or circulatory nephrosis is much better with proper management of the patient's water, electrolyte and nutritional requirements than is the prognosis of uremia due to severe acute glomerulonephritis. In the former case, circulation can still be reestablished in the glomeruli within two weeks or less; much tubular regeneration may occur. Very little can be done about polycystic kidneys directly, but fortunately in many cases, the destruction of renal tissue is slow enough to be compensated by hypertrophy of less involved nephrons. In practically all of the functional diseases of the kidney, appropriate therapy is of considerable value, provided the associated or underlying general disease or trauma does not in itself dominate the prognosis unfavorably. The prognosis of renal neoplasms and of various serious pyogenic infections of the kidney is almost entirely a function of early recognition.

## ACUTE DIFFUSE GLOMERULONEPHRITIS

In its acute form, acute diffuse glomerulonephritis is acute Bright's disease or acute hemorrhagic nephritis, characterized by the post infectious onset of gross hematuria, facial and other edema, hypertension, cerebral manifestations and changes in the blood and urine. The chronic form is simply a continuation of an unhealed, often unrecognized acute nephritis or its subsequent exacerbations.

*Etiology and Pathogenesis.*—The beta hemolytic Group A streptococcal infections account for at least three fourths of the cases of acute diffuse glomerulonephritis and by the same token for most cases of the residual chronic types of the disease. Usually the upper respiratory tract, including the accessory sinuses, is the focus of infection, but the focus of infection may be in the lungs, the seat of secondarily infected tuberculous cavities, bronchiectasis, suppurative pneumonia or lung abscess. It may also originate in pyogenic (streptococcal) infections of the skin such as impetigo, erysipelas, wound infections, ulceration of various types, and infected burns. The focus of streptococcal infection may in rare instances be in osteomyelitic bones, in infected lymph nodes in various parts of the body, or in the gastrointestinal or the genital tract. Other pyogenic organisms such as the pneumococcus, the streptococcus viridans and the non hemolytic streptococci

found on infected heart valves and in the blood stream in subacute bacterial endocarditis (and very rarely the gram negative pathogenic cocci) may be responsible for glomerulonephritis in a few cases The occurrence of true glomerulonephritis in bacillary infections or spirochetal septicemias has not been clearly established except for syphilis nor is there any evidence as yet of a possible viral origin of glomerulonephritis Acute glomerulonephritis as a result of oak sensitization has recently been discussed as a possibility by Rytand

The historical role of the chilling of the body in the etiology of acute glomerulonephritis is well established but must be reinterpreted as a predisposing factor to hemolytic streptococcal respiratory infections It is difficult however on this basis to explain cases in which hematuria and edema develop within a day or two of exposure to chilling or immersion Lacking accurate clinical data on the important matter of preceding respiratory infection the burden of proof lies with those who accept the coincidence at face value

Because of the prevalence of hemolytic streptococcal infections in children acute glomerulonephritis has its maximum incidence in the first two decades It may occur however at any age

The *pathogenesis* of glomerulonephritis is bound up in an immunologic reaction between a streptococcal kidney protein antigen of some sort and the corresponding autoantibody The combination of the antigen and its antibody in the glomerular endothelium presumably sets off the inflammatory reaction This theory is based largely on the Masugi experimental nephrotoxic nephritis and on *in vitro* demonstration by the Cavelti of autoantibodies to streptococcal kidney antigen There are serious objections however to applying the animal data to the human disease The immunologic theory is highly satisfying but still not conclusively proved The delay of at least a week or two between the acute streptococcal infection and the earliest clinical signs of nephritis so clearly documented in the older observations on scarlet fever nephritis is best explained by the time required to build up sufficient antibody for the allergic reaction in the kidney The parallelism to acute rheumatic fever is striking Yet though the same bacterial agent is involved and the antistreptococcal immunologic response is similar in the two diseases acute *glomerulonephritis is only infrequently associated* with acute rheumatic fever In the solution of this puzzle may lie the solution of the basic problem of selective localization of allergic responses to infection

*Symptoms and Course*—Acute diffuse glomerulonephritis may begin in the postinfectious period of a hemolytic streptococcal disease in a variety of ways There is the onset with vague lassitude headache a little nausea or anorexia perhaps some lumbar muscle pain and low fever (often attributed to the preceding infection) The erythrocyte sedimentation rate is elevated and there is often a polymorphonuclear leukocytosis of moderate degree If at this point the urine is examined carefully proteinuria and significant microscopic hematuria and cylindruria including some erythrocytic casts will be found These urinary changes also undoubtedly occur without any obvious symptoms and can be detected only by routine analysis the second week after an infection It is from this large group of nonspecific symptomatic or asymptomatic cases of acute glomerulonephritis that a great many cases of chronic nephritis of various types arise masquerading as idiopathic insidious or nonspecific chronic glomerulonephritis For every clear cut typical clinical case of acute glomerulonephritis there are probably at least ten subclinical cases most of them milder than the average full blown case

In the obvious case the disease may begin with gross hematuria or brown red smokiness of the urine puffiness of the face swelling of the feet and ankles or general increase in weight a noticeable reduction in urine volume at times a sensation of burning on urination headache (especially on awakening) nausea or vomiting general abdominal discomfort and distention dull aching or more severe pain over the lumbar regions In children projectile vomiting or generalized epileptiform convulsions may characterize the onset Cough difficulty in breathing palpitation oppression in the

chest or an acute attack of "asthma" together with great anxiety and profuse expectoration of pinkish frothy mucoid sputum, may develop early. Blurring of the vision, bleeding from the nose, or purpura of the skin may occur.

*Physical examination* will reveal a variable amount of waxy pallor, moon face with *swollen, translucent eyelids, both upper and lower and often, some edema of the scleral conjunctiva.* The tongue is usually coated and the breath may be foul or ammoniacal. The throat and tonsils may show evidence of recent inflammation and the *cervical lymph* nodes draining this region may be enlarged, tender or even fluctuant with pus (though this is extremely unlikely in these days of antibiotics). If the patient has had scarlet fever, erysipelas, impetigo, scabies or surgical wound infection, the appropriate skin lesions will be evident. The blood pressure may be normal or moderately or markedly elevated; the diastolic level may be disproportionately increased. The pulse may be hard and wiry, the heart rate either relatively slow with an elevated blood pressure *or more ominous increased.* The size of the heart is usually normal but in cases with signs of acute congestive failure, general enlargement may be found. The same is true of cases with pericardial effusion. The neck veins may be engorged and the antecubital venous pressure elevated. Orthopnea is common in both these situations. Deep breathing may be associated with acidosis but usually this does not occur during the first week. The heart tones may be normal, accentuated or distant depending on the associated conditions. Gallop rhythm of either type *is common in cases* with severe hypertension or signs of left ventricular failure. Other arrhythmias are unusual. The lungs are usually clear but *may show* residual bronchitic signs. Basal rales or generalized moisture is part of acute left-ventricular failure. The abdomen may be non contributory but on occasion is distended and tympanitic and may be tender in the epigastrium. In severe instances bowel sounds may be absent as the result of reflex or paralytic ileus. There may be moderate costovertebral tenderness and the kidneys may be palpable and sensitive. The liver is enlarged and tender in cases with congestive failure. The extremities may show a rather solid, tender edema, this edema may even involve the forearms and the hands. Reflexes are often hyperactive in the patients with hypertensive cerebral symptoms, and after convulsions, abnormal responses are obtained. Muscular hyperesthesia may be elicited in cases with profuse vomiting and dehydration. The ocular fundi are normal in the average case, but in patients with severe or sudden rises in blood pressure blurring or choking of the discs may develop *rapidly along with marked general narrowing* and localized transitory spasms of the retinal arterioles, venous engorgement, retinal edema, and striate hemorrhages. Subretinal detachment may occur after numerous convulsions.

The *urine* is usually grossly bloody or smoky or shows a frankly bloody sediment on standing or centrifugation. The volume is ordinarily reduced to 500 cc. or less for 24 hours but may still reflect the intake in mild or moderate cases. In severe inflammation of the glomeruli oliguria or anuria may set in within a few days. *Proteinuria* is usually marked but there are rare cases in which the proteinuria is only slight and sometimes even absent. The low salt content of the urine may interfere with the detection of traces of protein, hence a few drops of a saturated salt solution should be added to the urine before it is heated or the protein chemically precipitated. In addition to numerous erythrocytes and casts of all varieties, except for the doubly refractile lipoid type (never seen in the first few weeks of an initial attack of nephritis), there may be many *leukocytes, even in cast form.* The urine is usually strongly acid early and may show a high specific gravity in the first few days. Later even with oliguria the specific gravity falls, depending on the degree of renal tubular impairment. The persistence of a high specific gravity during oliguria in acute nephritis strongly suggests extrarenal dehydration, especially in the absence of edema.

*Kidney function* as measured by retention *in the blood of non protein nitrogen* and its individual fractions will usually show some *degree of impairment.* Glomerular filtration

is disproportionately reduced in relation to renal blood flow In severe oliguria uremic levels heightened by extrarenal factors may develop within a few days If the urine is bloody the PSP test is impractical otherwise it is a fairly sensitive measure both of the early impairment and of the early recovery stages The maximum urinary specific gravity or renal concentrating ability is quickly reduced in acute nephritis and is the last function to return to normal during recovery it lags weeks or months behind the PSP or urea-clearance test even when the patient is on a nearly normal diet as to protein and salt The renal excretion of water is usually not seriously impaired except in cases with severe oliguria although the response to a dilution test may be markedly delayed The excretion of salt is of course reduced whenever edema develops such reduction indeed is often the immediate cause of the edema In severe oliguria or anuria administered salt is completely retained and rapidly leads to increase in body fluids and circulatory embarrassment unless disposed of by abnormal extrarenal losses

During the course of acute glomerulonephritis three *complications* of major significance may arise hypertensive encephalopathy cardiac failure and uremia The first of these does not necessarily carry a serious prognosis the second does the last uremia is likely to be fatal

In *hypertensive encephalopathy* severe headache often general or occipital and associated with vomiting usually precedes the convulsive seizure In children the convulsion may apparently come out of a clear sky and be the first indication of glomerulonephritis after a streptococcal infection Visual disturbances blurring or scotomata or the seeing of flashes of light may precede or follow the seizure and may persist if hypertensive retinal edema develops The blood pressure is usually high or increases before the convulsion Convulsions may be repeated until serious or fatal circulatory or respiratory depression occurs Between seizures the patient may be comatose or semistuporous or restless and agitated and subject to mental aberration The temperature may rise considerably if the convulsions occur in short order Ordinarily however, the encephalopathic syndrome can be controlled by appropriate sedation

*Cardiac failure* in acute nephritis is most likely to occur in patients with mounting blood pressures or with sudden sharp hypertension and patients who continue to eat salted foods Left ventricular failure may occur suddenly as acute pulmonary edema with impending asphyxia The patient may turn ashen or livid with shock and die unless quickly treated for acute heart failure Acute hydropericardium or pericardial effusion along with hydrothorax may produce considerable dyspnea and venous congestion in acute nephritis This is usually of more gradual onset than acute left ventricular failure The picture of complete congestive heart failure with swollen tender liver engorged neck veins cyanosis and dilated heart with poor tones or gallop rhythm is found in patients with massive edema whose treatment has been neglected and in patients with acute myocarditis

*Uremia* in acute glomerulonephritis usually occurs after a few weeks of oliguria or several days of anuria Extrarenal components due to vomiting and diarrhea may be prominent and hypertensive encephalopathy or cardiac failure may be superimposed to produce a complicated situation In this type of uremia in contrast to that of chronic renal disease the patient s sensorium is usually not clear and the entire picture is more suggestive of a general toxemia Hemorrhagic phenomena are likely to develop in the skin the nasal and gastrointestinal mucous membranes the retina and the central nervous system A rapid anemia is common Acidotic breathing and coma compete with muscular twitchings and convulsions for the finale Once uremia has followed anuria in acute glomerulonephritis death almost always results

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*Prognosis* —The prognosis in acute diffuse glomerulonephritis depends on the patient s age the severity of the pathological process and functional impairment the heart s response to the strain of both the disease and its treatment and the time of recognition of the disease

Complete recovery from an initial attack of nephritis in childhood occurs in 90 per cent of the cases. The remaining 10 per cent include the acute cases of the disease and cases of uncured, hence eventually chronic, nephritis. When acute glomerulonephritis *first develops in adult life, the outlook for* complete recovery is on the average not better than 50 or 60 per cent and the incidence of unhealed chronic active nephritis approximates 30 or 40 per cent. The prognosis is much poorer in the rarer cases of initial acute nephritis in those past 50. Complete recovery probably never occurs *if the disease attacks kidneys already the seat of hypertensive or arteriosclerotic vascular* disease or senile atrophy.

When acute glomerulonephritis is so severe at the onset as to produce anuria apart from extrarenal factors or heavy globulinuria the pathology usually includes extensive obliteration of the glomerular capillaries by both endothelial proliferation and massive exudation and hemorrhage into *Bowman's capsule followed by extracapillary* epithelial and fibroblastic crescent formation. The prognosis is always grave in these cases because of the irreversibility of the process and the immediate depression of renal function.

*Cardiac failure*, whether left ventricular or general, is very serious in cases of acute nephritis and is responsible for about 25 *per cent of the deaths. It is dangerous not* only in itself but also through its hemodynamic effects on the renal dysfunction already present.

*Early recognition* of the disease through urinalyses after acute streptococcal infection leads to the institution of proper treatment, especially of bed rest. This may well prevent acute cardiac failure and other complications. *Whether early bed rest really has* much to do with complete recovery from early nephritis has recently been questioned by Rudebeck on a statistical basis. Most *observers agree* with Volhard, however, that chronic nephritis rarely develops in a patient put under medical care early during his initial attack of nephritis. Bed rest seems to be the chief reason for this, since various kinds of diet therapy have been used in conjunction with it and yet led to the desired result.

*Treatment.*—Bed rest and keeping the body warm are imperative until the major clinical signs and symptoms have disappeared. This usually takes several weeks *or months. The prevention of acute glomer*ulonephritis is based on the control of hemolytic streptococcal diseases, especially during mass exposure of susceptible children and young adults. Once a streptococcal sore throat is suspected, penicillin should be given immediately (300 000 units intramuscularly) and the dose repeated at intervals *of from 6 to 12 hours to suppress the antigen and the subsequent antibody* response. Repeated dosage of penicillin during the first few days of the infection is more important than the individual dose. The penicillin treatment of scarlet fever is based on a similar principle. When the antibiotic is given several times a day, antistreptolysin production can be completely suppressed and complications prevented.

*The prevention of some of the major* manifestations of acute nephritis—the vascular crises, heart failure, edema and nonprotein nitrogen retention—is a major concern. The common measure for the first three is the rigid dietary restriction of salt or sodium in any form. At the same time the fluid intake is limited to the volume of urinary output plus an allowance of from *500 to 1000 cc for normal extrarenal loss of* fluid. Sodium restriction prevents edema, delays cardiac failure and has an antihypertensive effect. Sedation with barbiturates, preferably those independent of renal excretion, or with 25 or 50 per cent *magnesium* sulfate given intramuscularly in repeated doses (controlled by frequent checks of the blood pressure, reflexes and respiratory rate) is valuable in preventing hypertensive seizures and reducing headache. Patients not subject to nausea may be given magnesium sulfate in doses of from 4 to 30 cc at the necessary intervals. Vasodilators of the *veratrum viride group* or papaverine given parenterally have also been successfully employed, the former may give rise to unpleasant gastrointestinal or circulatory reactions. Warm baths or diaphoretic procedures with proper replacement of

fluids lost by sweating have been relatively little used recently but can be fairly effective as a sedative and vasodilator procedure for patients with hypertensive symptoms Exposure to chilling and circulatory stress must be carefully avoided if hydrotherapy is employed

Prevention of non protein nitrogen retention becomes important in direct ratio to the severity of the acute nephritis and the degree of oliguria The goal is to reduce both protein intake and endogenous protein catabolism to a minimum This can be done by limiting the diet to carbohydrates and fats yet furnishing enough calories to prevent breakdown of body glycogen and protein or taking advantage of the protein sparing action of glucose In case of anorexia vomiting or inability to swallow because of stupor or coma intravenous glucose in 15 to 25 per cent solution is indicated Adequate vitamin B complex and vitamin C must always be administered with diets high in glucose The non protein nitrogen in the blood will still rise if there is severe oliguria but at a much slower rate Furthermore the acidosis caused by phosphates and sulfates associated with protein catabolism will be materially inhibited In the presence of anuria all electrolytes must be carefully excluded from the diet to prevent serious disturbances in body fluid volume or composition Specific electrolytes are given only to replace losses as indicated by chemical analysis of the serum

*Symptomatic treatment* in acute nephritis is a matter of relieving pain headache nausea vomiting insomnia and other minor symptoms by the usual simple measures In mild uncomplicated cases with good renal function only moderate restriction of dietary protein is indicated In the absence of hypertension or more than slight proteinuria rigid salt restriction is not necessary In severe cases one must consider the treatment of acute heart failure of generalized edema of respiratory distress or obstruction of oliguria and anuria of convulsions of acidosis and other electrolyte disturbances In addition to rigid or complete sodium restriction and sharp reduction of fluid intake the treatment for *acute cardiac failure* includes absolute bed rest in the semi upright posture for respiratory comfort the administration of oxygen by nasopharyngeal catheter or by mask or tent the administration of morphine or other hypnotic in adequate dosage venesection if the veins are acutely engorged the application of tourniquets to the limbs if anemia contraindicates blood removal the intravenous administration of digitalis glycosides or strophanthin preparations for rapid action on the myocardium This emergency cardiac treatment should not include aminophyllin or mercurial diuretic drugs These two potent agents are contraindicated in acute nephritis because the kidneys cannot respond to them and may be irritated or severely damaged by the drugs

The *edema* of acute glomerulonephritis may require treatment if extensive enough or in certain locations Obviously, restriction of sodium and fluid will limit the development of edema and will easily control it under average conditions Pleural fluid sufficient to embarrass respiration is rare but requires aspiration The same applies to the occasional ascites under tension Hydropericardium may be very difficult to distinguish from acute cardiac dilatation but when recognized may require tapping Edema of the glottis may require intubation or tracheotomy as an emergency Edema of the brain associated with hypertensive encephalopathy and increased intracranial pressure may necessitate cautious removal of spinal fluid (if this is done the danger of herniation into the foramen magnum must be borne in mind)

The treatment of *anuria* consists in attempting to restore urine formation while reducing the effects of urinary suppression on the metabolic processes Since prerenal or extrarenal dehydration or electrolyte depletion as the result of vomiting diarrhea or prolonged anorexia may at times be responsible for anuria in acute nephritis a careful history and appropriate serum chemical analyses are indicated This is particularly important in the absence of edema or pulmonary rales or the presence of slight edema and signs of dehydration In case of doubt it is permissible to administer up to 3 liters of fluid including one liter of physiological saline or saline plus lactate in

a ratio of 3 to 1, during the first twenty-four hours The response of the urinary output to this amount of fluid may reflect the presence of dehydration If there is no increase in urine volume no serious harm will have been done by the excess of fluid on one day If anuria persists for more than a few days the use of an "artificial kidney or dialyzing apparatus is definitely indicated, especially for hyperpotassemia provided an experienced group of physicians and the necessary facilities are available Otherwise it is essential to maintain the patient on carbohydrate and fat, without protein, without electrolytes of any sort unless symptomatic acidosis requires specific treatment, and on the minimal amount of water necessary to cover extrarenal losses

## CHRONIC DIFFUSE GLOMERULONEPHRITIS

When acute glomerulonephritis fails to clear up within a few weeks or months the possibility of chronic nephritis looms up to alter the prognosis Actually it is difficult to determine when the nephritis becomes chronic Residual microscopic hematuria and proteinuria may outlast other signs and symptoms of acute nephritis by months or even a year or two Until they disappear or are otherwise explained one cannot safely assume that the patient has recovered Once such recovery has occurred however permanent immunity is virtually assured for there are no authenticated cases of a second attack of glomerulonephritis It is therefore impossible to diagnose chronic glomerulonephritis within less than a year after the onset of the initial acute attack, unless gross symptoms and signs of active renal disease continue in addition to the urinary changes

Chronic glomerulonephritis is always an active process in the sense that it proceeds relentlessly, although at extremely variable rates While the term *latent* is often used loosely to designate a grossly asymptomatic chronic nephritis or, in the more exact sense a stage during which renal function blood pressure and urinary signs remain stationary or constant at any given level for some months or years, one should not be deceived by its apparently harmless connotation A latent chronic nephritis, properly defined does not proceed to healing, it simply moves more slowly than the more active types toward the inevitable stage of advanced renal insufficiency To avoid confusion and disappointment it is, perhaps, best not to think in terms of latent nephritis at all

*Etiology and Pathogenesis*.—Chronic glomerulonephritis is always the result of an unhealed episode of acute glomerulonephritis and therefore has the same etiology as the latter The inflammatory destruction of glomeruli, the atrophy of tubules and the secondary renal vascular changes combine to produce the various clinical forms

*Symptoms and Course*.—The patient with heavy proteinuria and reduced serum protein level will develop an edematous or *nephrotic* course and the associated nutritional and biochemical disturbances This will never be a pure lipoid nephrosis for there will always be evidence of glomerular inflammation in the urine even though the blood pressure and renal function as ordinarily determined may be normal In a few years the nephrotic type will develop into *mixed* chronic nephritis Ultimately the nephrotic edema and hypoalbuminemia may recede as renal insufficiency progresses and the patient enters the pre-uremic stage with moderately elevated or severely hypertensive levels of blood pressure The *hypertensive* non-edematous form of nephritis may be associated with relatively slow deterioration in renal function but is characterized eventually by the cardiac cerebral and retinal complications of hypertensive disease These may in turn accelerate the renal-disease process and final uremia In some patients the entire course of chronic glomerulonephritis is run with little edema or hypertension and with urinary findings of a minimal degree Nevertheless, after some decades severe renal impairment results These patients may not seek medical care or receive an accurate diagnosis for years because of the paucity of gross findings Nutrition may remain good because of lack of dietary restriction Yet anemia supervenes whenever renal failure has reached a sufficient degree of severity Growth and development in children may proceed normally in the pre-uremic stage

Otherwise some form of renal rickets or dwarfism may arise In the *course* of chronic glomerulonephritis *exacerbations* often occur which may be attributed to intercurrent infections usually hemolytic streptococcal or less clearly to renal hemodynamic disturbances secondary to minor or major surgery pregnancy trauma exposure or subjection to renal irritants Usually such an exacerbation is heralded by an increase in proteinuria and hematuria, gross or microscopic within a day or two of the precipitating factor A more gradual decrease in renal function may occur over a period of weeks a slow but often incomplete return toward the control level follows Edema rise in blood pressure headache malaise anorexia vague abdominal pain and some frequency of or irritation upon urination may or may not appear Only careful urine-sediment and renal function studies under controlled dietary conditions will reveal the true course of the disease

The course of chronic nephritis to uremia or other termination may be fairly rapid a matter of a few years or take from 2 to 4 decades especially if the onset occurs in childhood Since acute nephritis is essentially a disease of children and young adults it is unusual to encounter chronic glomerulonephritis even at autopsy past the age of 50

*Differential Diagnosis* —Chronic glomerulonephritis is to be distinguished from proteinuria and hematuria of non nephritic origin and from other forms of bilateral renal disease Only amyloid glomerulonephrosis and diabetic glomerulosclerosis can imitate the nephrotic type of nephritis in the adult Other characteristic findings in the first two diseases will serve to differentiate them from this nephrotic type In children the distinction between nephrotic nephritis and genuine nephrosis is not merely academic the latter carries a better prognosis than the former In genuine nephrosis there is complete absence of signs of glomerular inflammation and renal impairment over a fairly long period The differential diagnosis between chronic hypertensive nephritis and chronic pyelonephritis in later stages may be difficult in the absence of typical histories or abnormal pyelographic findings Yet the presence of doubly refractile lipoid cells and various types of casts in the urine will establish the diagnosis of chronic nephritis even when there is a confusing and superimposed infection of the lower urinary tract Similarly, anisotropic fatty cells and casts are not found in the urinary sediment of patients with essential hypertension or arteriolar nephrosclerosis In addition the combination of chronic hypertension and a normal urea clearance or other measure of glomerular filtration regardless of proteinuria is common in the earlier years or decades of essential hypertension and virtually unknown in chronic glomerulonephritis Polycystic kidneys are usually recognized on palpation or *x* ray The various types of chronic glomerulitis associated with general vascular diseases and chronic granulomatous infections should be differentiated from chronic glomerulonephritis as should the hypertensive renal toxemia of the last trimester of pregnancy Chronic congestive heart failure with severe passive congestion of the kidneys may imitate or obscure a more or less burned out' chronic glomerulonephritis Multiple myeloma occasionally enters the differential diagnosis of chronic glomerulonephritis because it may give rise to microscopic hematuria Tests for Bence-Jones protein in the urine *x* ray studies of the bones and aspiration of the bone marrow for myeloma cells will ordinarily settle the diagnosis Hyperparathyroidism rarely produces chronic renal insufficiency without nephrolithiasis or nephrocalcinosis but secondary hyperparathyroidism in chronic nephritis may produce a syndrome confusing even to the experts Finally bilateral renal vein thrombosis (a rare condition) may mimic the nephrotic syndrome or hypertensive nephritis with uremia

*Prognosis* —Recovery from chronic glomerulonephritis is always out of the question except in the few cases of the nephrotic type in children or young adults in whom no hypertension nor renal impairment is ever manifested Most chronic nephritics die of uremia About a third of the patients however die of cardiac failure or cerebral vascular accident before uremia sets in The prognosis of chronic glomerulonephritis is determined chiefly by the level of renal

function at the time of diagnosis and by the rate at which the disease progresses during the first few years

*Treatment* — Chronic glomerulonephritis should be prevented during acute nephritis Ideally, this should include some means of sharply reducing the amount of streptococcal antigen believed to initiate the immunologic chain in acute glomerulonephritis All patients with acute nephritis should be treated with penicillin or aureomycin until hemolytic streptococci are completely eradicated from the nose and throat or cutaneous foci Nitrogen mustard has been used experimentally to suppress the production of antibodies but its clinical effectiveness is still undecided although remissions of clinical activity of early chronic nephritis have been reported in a carefully studied but small series of cases (Chasis *et al*) Antihistaminic agents are of no value here nor has cortisone been demonstrated to be of value The importance of prolonged bed rest has been stressed

*Symptomatic* treatment of chronic nephritis is concerned with the maintenance of adequate nutrition within the limits of the renal functional capacity, and the management of edema or hypertension Apart from acute exacerbations the patient may be allowed ordinary reasonable physical activity without undue exposure to chilling He may engage in occupations not involving strenuous exertion or exposure to cold In the case of a woman pregnancy should be discouraged but may be permitted to continue if already under way provided renal function is only slightly reduced and the blood pressure only moderately elevated Any aggravation of symptoms should be an indication for interruption of pregnancy

The diet in chronic nephritis varies with the point of view of the physician For those who believe that *protein* is damaging to the kidney, a low protein diet (0 5 gm per kilo of body weight) with addition of extra protein for urinary loss or growth will be the regimen of choice even when renal function is still quite good However the administration of a more liberal diet containing from 0 7 to 1 gram of protein per kilo of body weight daily for the adult (and proportionately more for the nephritic child) is more practical and has not been shown to damage the kidneys There is higher proteinuria on diets high in protein than on diets low in protein but the difference is unimportant within the range of from 0 5 to 1 gm of protein per kilo of body weight a day and is far outweighed by the patient s improved nutritional status on the better diets When renal function falls to the preuremic level reduction of protein intake to the lower level (0 5 gm per kilo of body weight a day) is indicated

Apart from protein the diet in chronic nephritis should be normal unless the patient is edematous in which case the salt intake must be restricted Terminal uremic edema presents a very difficult problem for even water excretion is severely impaired at this point In dealing with low salt diets in *chronic nephritis, the problem of loss of* appetite and nutrition must always be weighed carefully against the possible benefits of the regimen The indiscriminate restriction of salt indicates a lack of understanding of how the kidney works It is *more important to maintain the patient s* tissues and strength than to follow traditional routine

Stubborn *nephrotic edema* necessitates a more liberal protein intake up to 1 5 grams per kilo of body weight a day for the adult *for restoration of the depleted body protein* It is however almost impossible to increase the serum albumin by increased protein in the diet as long as heavy proteinuria continues from damaged glomeruli A diet high in protein (more than 100 grams or so a day) *is useless here* It should be remembered that approximately 30 grams of tissue protein must be formed before 1 gram of serum protein is added It takes months on a good diet to bring about a significant rise in the serum protein concentration The *food protein should have* a high percentage of animal protein Adequate calories promote weight and prevent waste of protein energy must be furnished by carbohydrate and fat Since the lipemia and the hypercholesterolemia of the nephrotic syndrome are neither clearly related to nor influenced by the fat content of the diet there is no reason for restriction of lipids

The electrolyte disturbances in nephrotic edema associated with malnutrition may

involve low serum sodium increased serum chloride normal or low serum bicarbonate and variable serum potassium Tissue potassium depletion may exist and there is some reason to believe that sodium and chloride may be abnormally distributed in intracellular fluids All these changes justify the carefully controlled use of *mixtures of sodium and potassium* bicarbonate citrate acetate or lactate in amounts calculated to restore the normal electrolyte composition of the body fluids No hard and fast rules can be laid down for the exact amounts to be given since they depend on the biochemical findings before treatment and on the response to the administration of salt mixtures However renal insufficiency of significant degree excludes this type of treatment In successful instances diuresis and removal of edema may result in others alkalosis or hyperpotassemia may occur or temporary increase in edema This kind of treatment is not yet feasible for the general practitioner requires frequent serum and urine analyses Potassium salts should not be given if renal function is considerably impaired or oliguria is present and fails to respond to increased fluid intake

The use of *diuretic drugs* in nephrotic edema is not very successful but is indicated after empiric trial Purine drugs are of little value and soon cause gastrointestinal trouble and anorexia Potassium nitrate from 10 to 15 gram dosage daily may increase diuresis on a low fluid low salt intake and keep mild or moderate edema under control The organic mercurial diuretics with or without the synergistic effect of ammonium chloride or nitrate are not nearly so effective in nephrotic edema as in cardiac edema but should be tried unless there is considerable hematuria or other sign of fairly active or recent renal inflammation Renal function should not be less than 30 or 35 per cent of normal by the urea-clearance test and the maximal specific gravity corrected for proteinuria not less than 1 018 or 1 020 A good diuretic response is the best index of safety in the use of mercury in chronic nephritis

Attempts to elevate a very low serum albumin by means of concentrated plasma are impractical in adults because of the large amount required and the salt content In young children, however such attempts have sometimes succeeded The use of *salt poor human serum albumin* for this purpose is wasteful and expensive for most of the protein runs out into the urine Nevertheless it is indicated in very edematous anorexic and malnourished children to tide them over a bad period even if only temporary diuresis is obtained The harmlessness of repeated serum albumin injection is not entirely established

The use of *gum acacia* gelatin or other macromolecular solution for osmotic effects and diuresis in nephrotic edema has its advocates and opponents The occasional or intermittent infusion of these compounds is not dangerous and may be quite effective temporarily but the possibility of hepatic infiltration—with acacia for example if used repeatedly in quantity— must be borne in mind particularly in the case of children

In children there are two important complications of the nephrotic syndrome One is the *peritonitis* often pneumococcal complicating ascites and now readily controlled by *penicillin* The symptoms may not be dramatic therefore smears and cultures of peritoneal fluid should be made whenever the child has abdominal pain tenderness variable distention low fever or unusual anorexia or bowel disturbance The other complication is the metabolic state with signs of peritoneal irritation associated with a sharp fall in the amino-acid level of blood or plasma This *nephrotic crisis* ' is part of a severe nutritional change and can be alleviated promptly by the intravenous administration of amino acid mixtures or protein hydrolysates The possibility of potassium depletion in nephrotic children with persistent diarrhea must be remembered

*Hormone treatment* of nephrotic edema whether for diuretic or general effects has never measured up to the enthusiastic claims made for thyroid parathyroid testosterone and other products In the case of thyroid extract the large doses necessary for significant diuresis may give rise to diarrhea or have toxic effects Parathyroid hormone is not indicated for the reduced serum calcium attributable to low serum

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eventually lead to varying usually moderate, renal functional impairment and some degree of hypertension In the periarteritis nodosa or polyarteritis group the combination of glomerular inflammation and renal arteriolar or arterial disease may produce all the signs and symptoms of severe diffuse renal disease At times this renal involvement may furnish the first clue to the nature of a puzzling disease characterized by fever, wasting enlargement of the liver spleen and lymph nodes and negative results in tests for bacterial infection or lack of response to antibiotics In the chronic forms of focal glomerulitis careful and repeated search of the urine sediment for doubly refractile lipoid cells and casts will be rewarding and diagnostic

*Etiology and Pathogenesis* —The etiology and pathogenesis of focal glomerulitis vary with the responsible disease In the bacteriemias and septicemias, there may be bacterial or fibrin emboli focal capillary thrombotic lesions focal necrosis and reactive inflammation In the hyperergic vascular diseases the glomerulitis is presumably a local expression of a general vascular allergic inflammation comparable to foreign protein sensitization The fundamental nature of this reaction is still shrouded in mystery The net result however is glomerular capillary damage leading to hematuria and followed by healing or focal glomerular fibrosis If the glomerulus and its arterioles are sufficiently compromised the corresponding tubule will be rendered ischemic and undergo various types of degeneration and atrophy The effect on renal function will depend on the number of focal injuries to nephrons and the degree of final scarring

*Diagnosis* —The diagnosis is based on the association of some general infection or allergic disease with the typical urinary changes The chief problems in differential diagnosis are presented by acute or chronic diffuse glomerulonephritis and urinary tract bleeding due to blood dyscrasias urolithiasis tumors or other lesions from the renal pelves on down In general it is safest to consider diffuse glomerulonephritis as the basis for proteinuria hematuria and cylindruria until it can be reasonably excluded Many patients with ' focal nephritis have wound up with uremia some years later because they really had ordinary diffuse glomerulonephritis without early hypertension edema, or renal impairment Even subacute bacterial endocarditis classically responsible for focal embolic or thrombotic glomerulitis was associated in the pre-penicillin period with diffuse glomerulonephritis in about 10 per cent of the more prolonged cases

*Prognosis* —The prognosis in focal glomerulitis is determined by the underlying disease In acute bacteriemias complete cure is possible A few focally scarred glomeruli do no harm In subacute bacterial endocarditis serious renal damage may occur if the diagnosis is delayed After antibiotic therapy the patient may succumb to renal insufficiency from a combination of gross infarcts and glomerulitis of extensive nature In the allergic vascular diseases and visceral lupus erythematosus the glomerulitis and associated arteriolitis and arteritis may lead to uremia

*Treatment* —Treatment is not directed specifically at the glomerulitis but at the responsible disease or toxemia Antibiotics blood transfusions and hormones (*e g* ACTH or cortisone in visceral lupus) are used as indicated for the specific situation

## GLOMERULOSCLEROSIS—ARTERIOLAR (HYPERTENSIVE) AND DIABETIC

Glomerulosclerosis may be part of arteriolar nephrosclerosis secondary to essential hypertension or hypertensive renal vascular disease or may be the renal sequel of diabetes mellitus A combination of the two forms clinically and pathologically is common in the older age groups

## ARTERIOLAR GLOMERULOSCLEROSIS

Arteriolar glomerulosclerosis or nephrosclerosis usually has a background of essential hypertension It is therefore the most prevalent renal disease among older people

*Etiology and Pathogenesis* —The etiology varies with the theory of the physician as to

proteins, since the ionized calcium is usually adequate Testosterone may be beneficial in favoring nitrogen retention and formation of tissue protein, but its salt retaining action is a serious drawback unless the diet is very low in salt Reports of favorable results from cortisone are still too meager to warrant general use of this hormone in nephrotic nephritis If there is anything hormonal that the nephrotic patient needs it is either adrenocortical insufficiency with regard to salt and water-retaining hormones or increased adrenal production of a diuretic steroid

The treatment of the *hypertensive syndrome* in chronic glomerulonephritis is based, to a considerable extent on the same principles that underlie the management of essential hypertension even though the mechanism involved is probably different The removal of nervous and emotional stimuli to the vasomotor system is helpful in any type of hypertension so is the control of physical activity, obesity and other such factors However, since chronic nephritic or renal hypertension is supposedly humoral in origin sympathectomy is practically never indicated nor is it demonstrably effective in this condition As to the Kempner rice diet or other regimen very low in sodium it may have its value for hypertensive nephritic patients with edema and nitrogenous waste retention or in episodes of hypertensive encephalopathy and retinopathy but it is dangerous to employ for patients with a salt losing tendency That these diets have any beneficial effect on renal function *per se* remains to be established Vasodilator drugs apart from the relief of anginal pain or acute hypertensive headaches, are relatively unimportant in hypertensive nephritis It is essential however to follow the cardiac status closely and to deal as early as possible with impending left ventricular failure by employing digitalization, rest salt poor regimen, and other standard measures

*Anemia* is a frequent accompaniment of chronic nephritis If nutritional in origin it may be overcome with iron or protein supplements But if it results from severe protein depletion of the nephrotic stage the quickest and most effective way to combat it is by means of whole blood transfusions In the later stage of severe renal impairment anemia is partly due to the toxic depression of hemopoiesis Blood transfusions, repeated as necessary, offer the only way to make up this deficit The blood is best given in the form of packed red corpuscles to avoid overloading the circulation It is sufficient to maintain the hemoglobin at 70 or 80 per cent of normal to alleviate symptoms of anemia and of overwork on the part of the heart Meticulous typing and cross-matching are necessary for even a slight hemolytic reaction may prove very dangerous to a patient with renal function already at a low level In the hypertensive type of chronic nephritis, severe epistaxis or gastrointestinal bleeding may result The blood loss may require prompt replacement in the usual manner Very rarely prothrombin deficiency is a factor in the tendency to ecchymoses in the skin or mucous membranes in advanced renal insufficiency This is treated with vitamin K given parenterally or with fresh whole blood transfusions

## FOCAL GLOMERULITIS

Focal glomerulitis (focal glomerulonephritis) is really a pathological diagnosis and rather risky to make clinically if it is implied that it represents a rather harmless form of glomerular disease productive only of hematuria gross or microscopic without hypertension, edema or renal functional impairment In this chapter the term is used to include the glomerular lesions occurring in association with acute or chronic bacteremias allergic or hyperergic vascular diseases and the so called collagen diseases like visceral or disseminated lupus erythematosus The clinical expression of focal glomerulitis is hematuria with variable proteinuria and cylindruria Erythrocyte or blood pigment casts indicate the glomerular origin of the bleeding In the acute types the underlying disease usually a severe *acute infection or septicemia* is the dominant feature the renal involvement is detectable only by urinary study In the more chronic type—for example in subacute bacterial endocarditis and in visceral lupus—the progressive glomerular damage may

and Wilson is the specific renal disease of diabetics young and old. It is a major cause of death among diabetics. It causes death by way of uremia.

*Etiology and Pathogenesis*.—The etiology and pathogenesis are connected with diabetes and vascular disease in some unexplained manner. In young diabetics it usually takes some 15 or 20 years of the disease well or poorly controlled to culminate in the general vascular degeneration of which the renal arteriolar and glomerular changes are only a part. In older diabetics the exact duration of diabetes before the onset of renal involvement is undetermined and the frequency of coincidental hypertension increases the difficulty of the estimation. The glomerular hyaline ball degeneration of intercapillary glomerulosclerosis is directly diabetic in origin. Once the glomerular lesions develop the stage is set for proteinuria, lipoid degeneration of tubules and increasing renal insufficiency as glomeruli become obliterated and tubules atrophy. Desquamation of tubular epithelium laden with doubly refractile lipoid or cholesterol esters furnishes a valuable diagnostic criterion in the urinary sediment. Renal vascular changes are sufficient to produce hypertension.

*Symptoms and Course*.—In a known diabetic without a history of acute glomerulonephritis or abnormal hematuria the classical syndrome consists of marked proteinuria, hypoalbuminemia and hypercholesterolemia, moderate hypertension, diabetic retinopathy, nephrotic edema and fair or normal renal function. Actually this is a relatively rare combination of findings. More commonly the diabetic with hypertension and obvious retinopathy or peripheral vascular disease has proteinuria and edema not attributable to congestive heart failure or has proteinuria, anemia and renal insufficiency or uremia not explained by the common forms of bilateral renal disease. Other variations occur, including the absence of hypertension or of retinopathy. Even in patients with considerable proteinuria hypoalbuminemia is not a constant feature. The earliest signs of Kimmelstiel-Wilson disease are still unknown. Among older patients the diabetes may be latent and the renal disease suspected only because of the urinary findings. In these cases glucose tolerance tests are necessary for diagnosis of diabetes. On the other hand hypertensive and arteriosclerotic heart disease with congestive failure in older diabetics may effectively mask the diabetic glomerulosclerosis.

The course of the disease is usually only a matter of a few years. It progresses inevitably to uremia although cardiac, cerebral or peripheral vascular complications may be the immediate cause of death.

*Diagnosis*.—Diagnosis of Kimmelstiel-Wilson disease is relatively easy in the older age groups: proteinuria and edema appear in a diabetic without evidence of congestive heart failure or a valid background for amyloidosis (chronic suppurative tuberculosis, bronchiectasis or rheumatoid arthritis). The finding of doubly refractile lipoid cells and casts in the urine is virtually diagnostic. In dealing with the younger diabetics, usually in the third or fourth decade of life, many with histories of repeated respiratory or skin infection, the possibility of chronic glomerulonephritis must always be borne in mind. Active glomerulonephritis usually causes more hematuria than is indicated by the occasional red cells seen in the urine in diabetic glomerulosclerosis and the association of a normal urea clearance with chronic hypertension and urinary changes is most improbable in chronic glomerulonephritis but is possible in the earlier stages of diabetic glomerulosclerosis. Amyloidosis is also to be considered in younger diabetics but will present no serious problem if typically developed. The rare association of diffuse allergic vascular disease or visceral lupus erythematosus with diabetes may produce confusing renal findings but the general clinical features will ordinarily clarify the diagnosis. Diabetic glomerulosclerosis may be combined with pyelonephritis, necrotizing renal papillitis or infection of the lower urinary tract. In this last the characteristic urinary sediment changes of the Kimmelstiel-Wilson disease may be completely obscured by the pyuria and alkaline reaction of the urine. Even here the presence of noncardiac edema

the mechanism of hypertension in the middle and older age groups. Apart from the high incidence at autopsy of renal arterio- and arteriolosclerosis in victims of hypertensive disease and the much lower incidence in *renal biopsies obtained during dorsolumbar* sympathectomy on subjects with less advanced hypertension, nothing definite is known about the exact relationship between hypertension and renal vascular changes in man. The arteriolosclerosis of the afferent glomerular arterioles extends into the intraglomerular capillary branches, leading to gradual thickening and hyalinization of the walls and obliteration of vascular channels. Ultimately, the entire glomerulus becomes hyalinized, sclerotic and useless, the corresponding tubule is deprived of blood supply and atrophies. The process may be very gradual in a few cases, however, it may be accelerated to a necrotizing arteriolitis and glomerulitis with microscopic infarction of nephrons and rapid destruction of kidney tissue and function. This process often affects simultaneously small vessels elsewhere in the body (*e g*, in the brain, in the adrenals, the pancreas, the gastrointestinal tract and the retina). This is malignant nephrosclerosis pathologically or malignant hypertension clinically, but the two terms are far from synonymous since they are based on different sets of criteria.

*Symptoms and Course* —The *symptoms* are those of the hypertensive syndrome. The urinary findings are these: proteinuria mild to moderate, a few if any erythrocytes (except in arteriolonecrosis), some hyaline and granular casts in the sediment. The maximal specific gravity of the urine may be normal at first (though ordinarily somewhat reduced) but eventually becomes fixed at the isosthenuric level. There is no edema until cardiac failure occurs. Renal functional impairment indicative of diminished tubular mass and excretory ability and reduced renal blood flow with relatively well preserved glomerular filtration (hence an increased filtration fraction) are usually found by the special clearance tests at this stage. The urea clearance may be within lower normal range, unlike the situation in chronic hypertensive glomerulonephritis. Left-ventricular enlargement, left-ventricular-strain pattern in the ECG, and signs of hypertensive retinopathy are ordinarily observed by the time the renal signs of hypertensive disease appear. Cerebral vascular damage of varying degree may be found at this stage. The increasing renal insufficiency may terminate in uremia, but this occurs in only 10 or 15 per cent of the cases, the rest of the hypertensives succumb chiefly to cardiac failure, coronary or cerebral accident, or intercurrent infection.

*Diagnosis* —The diagnosis of nephrosclerosis is readily made when chronic hypertensive disease and urinary changes are found. Chronic pyelonephritis with hypertension can usually be distinguished from nephrosclerosis from the history in the former of urinary tract infection, obstruction, pyuria and bacteriuria, and pyelographic abnormality. In some cases, however, no positive criteria may be available, although renal function is likely to be more impaired in pyelonephritis than in nephrosclerosis. It is important, particularly in younger persons with severe hypertension and retinopathy, to consider the possibility of unilateral atrophic pyelonephritis. Pheochromocytoma with nonparoxysmal hypertension and urinary abnormality is a rare disease but must be kept in mind and tested for by means of benzodioxane. The Cushing syndrome will present other obvious features besides hypertension, proteinuria and renal impairment. However, obesity and essential hypertension are often combined and even diabetes and amenorrhea may be thrown in for good measure without necessarily implicating the adrenal hyperfunction of the *Cushing syndrome*. Polycystic kidneys when not readily palpable may cause confusion in diagnosis.

*Treatment* —Treatment of arteriolar glomerulosclerosis consists in the management of hypertension and renal dysfunction. The latter requires no special care until considerable renal insufficiency has developed. In most cases the real therapeutic problem will be cardiac or cerebral in origin.

## DIABETIC GLOMERULOSCLEROSIS

Diabetic glomerulosclerosis or the intercapillary glomerulosclerosis of Kimmelstiel

sive mechanism This however is unusual in amyloidosis the cachexia and the concurrent involvement of the liver and the adrenals are much more likely to be associated with arterial hypotension Once heavy proteinuria has set in the rest of the nephrotic syndrome is a logical sequence in amyloid glomerulonephrosis It is modified however, by the nutritional and metabolic aberrations associated with the primary disease Involvement of the heart muscle in primary amyloidosis may cause cardiac failure

*Symptoms and Course* —Amyloid glomerulonephrosis may be characterized by proteinuria and cylindruria a complete nephrotic syndrome, a mixture of nephrotic and uremic manifestations or undiluted asthenic uremia The renal symptoms may be confused with clinical expressions of the underlying disease or with the effects of amyloid deposition in liver adrenals myocardium gastrointestinal tract bone marrow and elsewhere Weakness emaciation hypotension anemia pigmentation and gastrointestinal disturbances are common in well-established amyloid nephrosis Anorexia and a reduced salt intake will limit the amount of edema Hypercholesterolemia is often absent owing to cachexia caused by the underlying disease A positive result in the Congo red test will be obtained if there is general amyloidosis the result may be doubtful if the kidneys are chiefly involved or the amyloid is atypical The urine may contain considerable serum globulin in addition to serum albumin In cases with more tubular than glomerular dysfunction no edema is observed On the contrary the salt losing type of renal disease may develop with electrolyte depletion and dehydration and mimic the syndrome of adrenal cortical insufficiency

The *course* of amyloid nephrosis depends on the degree of renal functional impairment at the time of diagnosis and on the nature and activity of the underlying disease Proteinuria may exist for some years before more serious signs appear Once renal insufficiency is obvious the disease lasts about two years or less unless a striking improvement in the causative condition can be effected The *prognosis* in renal amyloidosis is poor once the disease is fully established

*Diagnosis* —Diagnosis of renal amyloidosis is easy in the average case in a child or young adult with a disease furnishing a background for amyloidosis Chronic glomerulonephritis is readily excluded by the absence of significant hematuria and hypertension and by the presence of proteinuria out of all proportion to the number of casts or epithelial cells In children orthostatic or postural proteinuria must be considered in the differential diagnosis of early stages of amyloid glomerulonephrosis In older patients especially those with arteriosclerotic heart disease and congestive failure the finding of doubly refractile lipoid cells or casts in the urine sediment will be diagnostically helpful if diabetes can be excluded The Congo red test is of value in diagnosing renal amyloidosis in older persons In general, differential diagnosis of the renal involvement is facilitated if there is reason to suspect amyloid deposition in the liver and spleen Biopsy of the liver often establishes the diagnosis Biopsy of the gums may reveal amyloid in a few cases

*Treatment* —Treatment consists primarily in eradicating or sterilizing chronic foci of suppuration in the lungs the bones the joints and elsewhere The maintenance of optimal nutrition on diets high in protein and in vitamins and the control of anemia also help prevent amyloid formation and deposition

As for *symptomatic treatment* the usual measures for control of edema hypoproteinemia and azotemia are instituted

Due allowance is made for the general nutritional status which is often quite poor It has been held that the parenteral administration of large amounts of liver extract preferrably in the crude form in addition to the use of diets high in protein has cleared up amyloidosis including the renal deposits It is certainly established that the liver and spleen can reabsorb amyloid completely under proper conditions Whether this also holds for the kidney is not clear

## LIPOID GLOMERULONEPHROSIS

*Lipoid glomerulonephrosis* or "genuine" lipoid nephrosis is a disease of infants and

should lead the physician to suspect glomerulosclerosis.

*Treatment.*—Treatment of glomerulosclerosis consists in the prevention of diabetes mellitus, wherever possible, through the control of obesity and other predisposing factors.

*Symptomatic treatment* of diabetic glomerulosclerosis includes the standard treatment of diabetes mellitus and the individual symptoms of the renal complication. In regard to the diabetes, it must be noted that increasing renal impairment tends to reduce glycosuria by diminished glomerular filtration. Hence, the insulin requirement becomes smaller and hyperglycemia is common without glycosuria. Attempts to keep the blood glucose in the normal range by extra insulin doses are likely to cause serious hypoglycemic reactions and should be discouraged. In some patients no insulin need be given. The absence of glycosuria does not mean that ketosis and ketonuria are absent. They should always be tested for. The diet is kept low in salt, as for cardiac cases, if the patient has significant edema. The normal protein intake in the diabetic diet is adequate to cover the proteinuria in most cases of diabetic glomerulosclerosis. In those with 20 or more grams of protein in the 24 hour urine, supplementary dietary protein is indicated. However, patients with glomerulosclerosis seem to maintain their plasma-albumin levels with less difficulty than the nephrotic glomerulonephritic patient. When renal impairment reaches the point of considerable nonprotein nitrogen retention, appropriate reduction in protein intake and increase in fluids intake are indicated. Cardiac failure is treated as usual. The use of mercurial diuretics should be avoided unless the level of renal function is more than 30 per cent by the urea clearance test and the patient responds to a test dose. The use of ammonium chloride or other acid forming salts as diuretic adjuvants must also be avoided if there is considerable renal insufficiency. The mobilization of edema in diabetic glomerulosclerosis may be most difficult because of the combination of four factors antagonistic to diuresis—renal excretory failure, cardiac insufficiency, anemia, and hypoproteinemia. Mechanical removal of edema fluid from body cavities and subcutaneous tissues is employed where other measures fail. The liability of diabetics to urinary-tract infections makes it imperative to culture the urine frequently and to use antibiotics liberally. Insulin resistance may be an aggravating factor in rare cases.

## GLOMERULONEPHROSIS

The glomerulonephroses are amyloid nephrosis, lipoid nephrosis, and the nephrosis of pregnancy.

### *AMYLOID GLOMERULONEPHROSIS*

Amyloid glomerulonephrosis is usually part of general amyloidosis, whether secondary or primary in type, although it may occasionally represent the major amyloid deposit in the body. Its incidence is diminishing rapidly because of better surgical treatment of chronic suppuration in bones and lungs and antibiotic therapy of infections. The cortisone and ACTH treatment of rheumatoid arthritis may, in the future, still further reduce the incidence of renal amyloidosis.

*Etiology and Pathogenesis.*—The etiology and pathogenesis of amyloid glomerulonephrosis are part of the unsolved problem of amyloidosis in general. The role of hyperglobulinemia in producing amyloidosis is unproven and there are striking discrepancies in the alleged association. In secondary amyloidosis, related to chronic suppuration, rheumatoid arthritis and the lymphomas (Hodgkin's disease and multiple myeloma), the kidney is regularly involved. The amyloid is deposited in the glomeruli and the membrana propria of the tubules. The glomerular permeability for serum protein is increased; later filtration is reduced by the encroachment of the amyloid on the capillaries. Eventually complete obstruction to blood flow occurs; hyaline fibrosis follows. Corresponding tubular ischemia, degeneration, atrophy, and replacement fibrosis lead to increasing tubular functional impairment. Among older patients, though seldom among younger ones, without a wasting disease, sufficient renal vascular involvement may occur to set off the humoral hyperten-

sive mechanism This, however, is unusual in amyloidosis the cachexia and the concurrent involvement of the liver and the adrenals are much more likely to be associated with arterial hypotension Once heavy proteinuria has set in the rest of the nephrotic syndrome is a logical sequence in amyloid glomerulonephrosis It is modified however by the nutritional and metabolic aberrations associated with the primary disease Involvement of the heart muscle in primary amyloidosis may cause cardiac failure

*Symptoms and Course* —Amyloid glomerulonephrosis may be characterized by proteinuria and cylindruria a complete nephrotic syndrome a mixture of nephrotic and uremic manifestations or undiluted asthenic uremia The renal symptoms may be confused with clinical expressions of the underlying disease or with the effects of amyloid deposition in liver adrenals myocardium gastrointestinal tract bone marrow and elsewhere Weakness emaciation hypotension anemia pigmentation and gastrointestinal disturbances are common in well established amyloid nephrosis Anorexia and a reduced salt intake will limit the amount of edema Hypercholesterolemia is often absent owing to cachexia caused by the underlying disease A positive result in the Congo red test will be obtained if there is general amyloidosis the result may be doubtful if the kidneys are chiefly involved or the amyloid is atypical The urine may contain considerable serum globulin in addition to serum albumin In cases with more tubular than glomerular dysfunction no edema is observed On the contrary the salt losing type of renal disease may develop with electrolyte depletion and dehydration and mimic the syndrome of adrenal cortical insufficiency

The *course* of amyloid nephrosis depends on the degree of renal functional impairment at the time of diagnosis and on the nature and activity of the underlying disease Proteinuria may exist for some years before more serious signs appear Once renal insufficiency is obvious the disease lasts about two years or less unless a striking improvement in the causative condition can be effected The *prognosis* in renal amyloidosis is poor once the disease is fully established

*Diagnosis* —Diagnosis of renal amyloidosis is easy in the average case in a child or young adult with a disease furnishing a background for amyloidosis Chronic glomerulonephritis is readily excluded by the absence of significant hematuria and hypertension and by the presence of proteinuria out of all proportion to the number of casts or epithelial cells In children orthostatic or postural proteinuria must be considered in the differential diagnosis of early stages of amyloid glomerulonephrosis In older patients, especially those with arteriosclerotic heart disease and congestive failure the finding of doubly refractile lipoid cells or casts in the urine sediment will be diagnostically helpful if diabetes can be excluded The Congo red test is of value in diagnosing renal amyloidosis in older persons In general differential diagnosis of the renal involvement is facilitated if there is reason to suspect amyloid deposition in the liver and spleen Biopsy of the liver often establishes the diagnosis Biopsy of the gums may reveal amyloid in a few cases

*Treatment* —Treatment consists primarily in eradicating or sterilizing chronic foci of suppuration in the lungs the bones the joints and elsewhere The maintenance of optimal nutrition on diets high in protein and in vitamins and the control of anemia also help prevent amyloid formation and deposition

As for *symptomatic treatment* the usual measures for control of edema hypoproteinemia and azotemia are instituted

Due allowance is made for the general nutritional status which is often quite poor It has been held that the parenteral administration of large amounts of liver extract preferrably in the crude form in addition to the use of diets high in protein has cleared up amyloidosis including the renal deposits It is certainly established that the liver and spleen can reabsorb amyloid completely under proper conditions Whether this also holds for the kidney is not clear

## LIPOID GLOMERULONEPHROSIS

*Lipoid glomerulonephrosis* or genuine lipoid nephrosis is a disease of infants and

young children characterized by the nephrotic syndrome without any of the other signs of glomerulonephritis Remissions and relapses are common but complete cure occurs in about half the cases even after years of the disease Occasionally, the disease is active for more than a decade and results in renal insufficiency secondary to gradual tubular atrophy and replacement fibrosis Before the days of chemotherapy and antibiotics death often resulted from intercurrent infection particularly erysipelas or cellulitis of the edematous skin peritonitis in the presence of ascites and nutritional crises associated with hypoaminoacidemia and liver dysfunction Curiously enough some of the most striking remissions and permanent cures in cases of this disease have followed acute infections of all sorts especially measles *This has actually led to the deliberate induction of measles in nephrotic children with very stubborn edema and ascites*

*Etiology and Pathogenesis* —To those who believe that there is no such thing as pure or genuine lipoid nephrosis that it is always a variant of mild chronic glomerulonephritis in which the inflammatory element is at a minimum the etiology is clear and the pathogenesis similar to that of the parent disease However, the existence of a clinical and pathological complex of a specific type is well established There are two theories the first that the abnormal glomerular permeability to serum albumin is the expression of a degenerative process limited initially at least to the kidney the second that the renal changes are merely part of a general metabolic disorder involving protein synthesis and related processes According to the first theory proteinuria leads to reduction in the serum proteins nephrotic edema tissue protein breakdown lipemia susceptibility to infections and other features of true nephrosis According to the second theory, the edema and the hypoalbuminemia are not directly related to the proteinuria but, respectively to the altered metabolic and sodium reabsorptive activity of the renal tubules and the abnormal protein synthesis The two views are not irreconcilable The actual etiology of the glomerular change is not known it is not so clearly related to streptococcal or other infection as is glomerulonephritis, but there seems to be some relationship There is some clinical evidence to support the view that certain drugs, like tridione and sensitizing agents like poison oak, may be causal factors The tubular degeneration so striking in the pathology of the kidney in nephrosis is presumably largely the effect of the accumulation of lipids (cholesterol esters especially) in the epithelium of the convoluted tubules These deposits apparently derive to a considerable extent from plasma material filtered through the damaged glomeruli *The functional capacity of the* glomeruli and the tubules remains strikingly unimpaired, except for the reduced excretion of salt and water Even this is simply an expression of excellent reabsorptive activity

*Symptoms and Course* —The symptoms and course are very much like those of nephrotic nephritis, except for the more insidious onset and more stubborn course Generalized edema of the waxy type, effusions into body cavities and tissue wasting masked by the inflated appearance of the nephrotic child, form a striking and unforgettable picture Anorexia, vomiting and diarrhea of a watery type are common in the severely edematous patient Secondary anemia is to be expected as are vitamin deficiencies The tense water laden skin is easily broken and subject to cellulitis Edema of the external genitalia may interfere with urination Swelling of the eyelids may be a source of annoyance and conjunctival edema may result in irritation The edema is usually soft, freely movable and non tender It affects the face the scalp and the arms Dehydration due to anorexia and gastrointestinal disturbance may be combined with the edema This may lead to cerebral symptoms a shocklike state and prerenal azotemia with variable electrolyte disturbances Ordinarily in the nephrotic child the serum sodium is low normal the serum CO reduced and the chloride elevated

The *urine* is often highly concentrated and alkaline except during diuresis Protein casts and epithelium including many doubly refractile lipoid cells also found in casts are present in the urine The

protein concentration in the urine may reach 4 or 5 per cent and the 24 hour loss often reaches 10 or 20 grams about 90 per cent in the form of albumin Fine chemical, electrophoretic and immunologic distinctions between the serum and urinary proteins of nephrosis and the normal serum proteins can be demonstrated but their exact significance is unknown The changes may represent basic alteration in the protein regenerating mechanism or the result of rapid loss and rapid regeneration and lack of time for complete maturation of the various fractions The latter possibility is supported by the fact that the serum proteins rapidly return to normal whenever a remission in the disease is accompanied by a striking reduction in or cessation of proteinuria That the lipemia and the hypercholesterolemia of nephrosis should be accompanied by a rise in the beta globulin fraction of the serum is not surprising Perhaps the low resistance to infection is in keeping with the usually low level of gamma globulin in nephrosis

The results of the ordinary *renal function tests* are normal in nephrosis but water excretion in the dilution test is considerably delayed The urea nitrogen in the blood is normal but varies with the level of protein in the diet and the fluid intake The glomerular filtration rate is not only normal but often considerably elevated as is the renal blood flow Tubular maximal excretory capacity for diodrast and p aminohippurate may also be increased markedly The explanation for these remarkable changes is not apparent These supernormal values are readily induced in young nephrotic children by diets high in protein All these functional changes are in a different direction for those seen in nephrotic glomerulonephritis There is some evidence of increased antidiuretic material in the urine this suggests an excess of hormonal activity on the distal tubule

The *course* of lipoid glomerulonephrosis is characteristically one of remissions and relapses After months of stationary or increasing edema—edema resistant to all ordinary measures and accompanied by heavy proteinuria serum albumin levels often below 1 5 grams per cent and blood protein levels well below 4 per cent—sudden diuresis may set in spontaneously Luetscher has found a significant increase in plasma volume an early signal of this diuresis An intercurrent infection of almost any type may be associated with a relapse into the edematous state or with a sharp decrease in the proteinuria and a rapid disappearance of the edema followed by a gradual rise in the serum proteins The most dramatic remissions seem to have occurred at the height of the eruption of measles In fact a number of authentic cures of nephrosis have been reported after this infection In most cases however relapse takes place after a few weeks or months Massive edema effusion of fluid into the body cavities malnutrition due to anorexia tissue wastage and marked proteinuria render the nephrotic child unusually susceptible to pneumococcal streptococcal and other infections of the respiratory tract the skin and the peritoneum In the presulfonamide days such infections often proved fatal though renal function was still excellent Pyrexia and abdominal pain tenderness and rigidity should arouse the suspicion of peritonitis (usually pneumococcal) The peritoneal fluid should be aspirated and smears and cultures of it made Sudden fever prostration listlessness pallor nausea severe abdominal or flank pain with distention and rapid grunting respiration may indicate a *nephrotic crisis* of metabolic origin related to a low plasma amino acid level (less than 2 5 mg per 100 cc by the ninhydrin method) of sudden or gradual development These attacks last only from 12 to 48 hours unless complicated by infection

*Differential Diagnosis* —Lipoid glomerulonephrosis is chiefly to be distinguished from nephrotic glomerulonephritis The absence of hematuria in highly concentrated acid urine is the most differential sign

Any elevation of blood pressure or sign of persistent renal functional impairment not due to pre renal factors should make one very skeptical of a diagnosis of nephrosis Amyloid nephrosis is usually readily excluded by its background of suppurative disease and evidence of hepatic and splenic

young children characterized by the nephrotic syndrome without any of the other signs of glomerulonephritis. Remissions and relapses are common, but complete cure occurs in about half the cases even after years of the disease. Occasionally, the disease is active for more than a decade and results in renal insufficiency secondary to gradual tubular atrophy and replacement fibrosis. Before the days of chemotherapy and antibiotics, death often resulted from intercurrent infection, particularly erysipelas or cellulitis of the edematous skin, peritonitis *in the presence of ascites*, and *nutritional* crises associated with hypoaminoacidemia and liver dysfunction. Curiously enough, some of the most striking remissions and permanent cures in cases of this disease have followed acute infections of all sorts, especially measles. This has actually led to the deliberate induction of measles in nephrotic children with very stubborn edema and ascites.

*Etiology and Pathogenesis.*—To those who believe that there is no such thing as pure or genuine lipoid nephrosis, that it is always a variant of mild chronic glomerulonephritis in which the inflammatory element is at a minimum, the etiology is clear and the pathogenesis similar to that of the parent disease. However, the existence of a clinical and pathological complex of a specific type is well established. There are two theories: the first, that the abnormal glomerular permeability to serum albumin is the expression of a degenerative process limited, initially at least, to the kidney; the second, that the renal changes are merely part of a general metabolic disorder involving protein synthesis and related processes. According to the first theory, proteinuria leads to reduction in the serum proteins, nephrotic edema, tissue protein breakdown, lipemia, susceptibility to infections and other features of true nephrosis. According to the second theory, the *edema and the hypoalbuminemia* are *not* directly related to the proteinuria but, respectively, to the altered metabolic and sodium reabsorptive activity of the renal tubules and the abnormal protein synthesis. The two views are not irreconcilable. The actual etiology of the glomerular change is not known. It is not so clearly related to streptococcal or other infection as is glomerulonephritis, but there seems to be some relationship. There is some clinical evidence to support the view *that certain drugs, like tridione, and sensitizing* agents, like poison oak, may be causal factors. The tubular degeneration so striking in the pathology of the kidney in nephrosis is presumably largely the effect of the accumulation of lipids (cholesterol esters especially) in the epithelium of the convoluted tubules. These deposits apparently derive to a considerable extent from plasma *material filtered through the damaged* glomeruli. The functional capacity of the glomeruli and the tubules remains strikingly unimpaired, except for the reduced excretion of salt and water. Even this is simply an expression of excellent reabsorptive activity.

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The *urine* is often highly concentrated and alkaline except during diuresis. Protein, casts and *epithelium*, including many doubly refractile lipoid cells, also found in casts, are present in the urine. The

cence Or the fever may be irregularly continuous with severe prostration stupor or mental confusion Dehydration may develop rapidly in children especially when diarrhea is one of the early symptoms Abdominal distention with other signs of paralytic ileus may occur There is often marked costovertebral tenderness or sensitivity to percussion over this area It may be much more marked on one side than on the other The kidneys may be palpable enlarged and tender Stretching of the iliopsoas muscle may aggravate the pain in the flank or abdomen A moderate leukocytosis with increase in polymorphonuclears and a shift to the left is common Anemia may develop rapidly even to the point of slight icterus In the severe types signs of general toxemia are evident Bacteriemia is often found when blood is taken for culture from a patient undergoing a chill Enlargement and tenderness over the liver and spleen result The chemical blood changes usually reflect the increased protein catabolism dehydration and a variable degree of renal impairment

The *urine* early is concentrated and usually turbid or cloudy The reaction is usually acid with E coli and streptococcal infections but is alkaline in infections due to urea-splitting staphylococci B proteus and related bacteria It shows moderate protein content a purulent sediment and often bacteria on direct smear A variable number of erythrocytes is also present but not in cast form Gross hematuria may be seen The leukocytes are found typically in clumps and sometimes massed in casts Granular and epithelial casts may also be present However there are cases in which for a few days there may be very little pus in the urine this is due either to failure of the interstitial exudates to extend into the renal excretory ducts or what is more serious to obstruction of the renal pelvis or ureter by a plug of coagulated pus Culture of the urine will reveal the offending bacteria and is an essential part of the examination of the patient

The *course* of an acute pyelonephritis is ordinarily self limited to a few days or one or two weeks even without specific treatment provided there is no serious obstruction of the urinary tract If the patient stays in bed and is able to retain enough fluids to irrigate his urinary channels the acute infection sooner or later subsides and there may be no residual damage nor may there be recurrence of the disease However retention of purulent exudate in the renal pelvis may lead rapidly to a pyonephrosis or generalized septicemia In some instances the renal parenchyma is seeded with numerous miliary abscesses and grossly purulent infiltrates In these cases the clinical picture is a combination of severe infection and toxemia and increasing renal insufficiency This is particularly likely to occur in ascending infections from obstructed or paralytic bladders but may also result from hematogenous staphylococcal infection in patients with furuncles or osteomyelitis Extension of suppuration through the capsule of the kidney may result in perinephritic abscess Septic emboli from infected renal veins will lodge in the lungs to produce suppurative pneumonitis or infarct formation

*Diagnosis* —There is usually no difficulty in diagnosis of acute pyelonephritis if one remembers to consider this condition in any patient of any age with otherwise unexplained fever abdominal symptoms or urinary-tract signs In infants and children it is one of the major causes of febrile infection Any patient with known urolithiasis urinary stricture enlarged prostate or any congenital anomaly of the urinary tract capable of causing obstruction is potentially a candidate for acute pyelonephritis The differential diagnosis from other common causes of fever and abdominal pain is based largely on the typical urinary findings including the important urine cultures Intravenous pyelography may be very useful in disclosing the underlying obstructive lesion especially in cases with unilateral pain and upper abdominal tenderness when distinction from acute gall bladder disease may be difficult Differentiation from acute glomerulonephritis is ordinarily easy because of the absence of edema hypertension and erythrocyte casts However since in glomerulonephritis there may be little hypertension or edema and the urine may contain leukocytes in addition to the other findings

until recovery has occurred. Future pregnancies are not contraindicated if renal function, the urine, and the blood pressure remain normal.

## PYELONEPHRITIS OR PYOGENIC INFECTIONS OF THE KIDNEYS

Pyogenic renal infections constitute the largest and most important group of organic renal diseases. Fortunately, they are the most susceptible to specific therapy.

### ACUTE PYELONEPHRITIS

Acute pyelonephritis is the most common of the diffuse renal diseases. It is caused by a variety of pyogenic bacteria. It often reveals an underlying urinary tract obstruction or anomaly.

*Etiology and Pathogenesis.*—Any microorganism capable of producing suppurative inflammation may lodge in the kidneys and initiate acute pyelonephritis. The bacteria usually responsible for pyelonephritis are the gram negative bacilli of the E. coli group, A. aerogenes, B. proteus, Pseudomonas aeruginosa, and various enterococci. Staphylococci may also be involved. Mixed infections are common in recurrent or chronic cases. The tubercle bacillus is an important cause of specific pyelonephritis and must always be considered when urinary tract infection exists in the presence of urine sterile for ordinary pathogens. Organisms like E. typhosa may pass through the kidney into the urine without producing any renal inflammation of note.

The theory of ascending infection of the renal pelvis and parenchyma is apparently supported by the incidence of pyelitis or pyelonephritis after urethritis, prostatitis and cystitis, especially when instrumental examination or urethral catheterization has been carried out. However, even in these cases there is good reason to believe that traumatic bacteriemia has occurred. The influence of pregnancy in producing hormonal and mechanical stasis in the ureter predisposes to pyelonephritis.

Microorganisms ordinarily reach the kidneys via the circulation, multiply in the interstitial tissue around the glomeruli and tubules, and set up reactions varying from inflammatory edema and leukocytic infiltration to massive suppuration and extension of inflammation to adjacent structures. Secondary invasion of renal venous channels and lymphatics spread the infection throughout the circulation. Less frequently bacteria invade the kidney along the lymphatics from the lower urinary or adjacent bowel tract or, in neurogenic bladders, by direct reflux of infected bladder urine. The suppurative process in the kidney usually breaks into the collecting ducts and involves the renal pelvis—pyelitis is nearly always part of a pyelonephritis—and purulent material may obstruct the calyces or ureter to produce serious consequences. The interstitial inflammation extends to the blood vessels and leads to thrombophlebitis and arteritis. The latter may be responsible not only for ischemic necrosis or atrophy of renal parenchyma but, under appropriate circumstances, for the release of the Goldblatt pressor mechanism to produce an intermittent, chronic or accelerated malignant hypertension. Varying degrees of renal insufficiency result from these processes but this feature of pyelonephritis is usually not important until a long period has elapsed. There are infrequent instances of acute interstitial pyelonephritis with severe edema of the kidneys, high intrarenal tension and oliguria sufficient to produce acute uremia. The inflammatory process may be asymmetrical and productive of unilateral atrophy.

*Symptoms and Course.*—In children and young adults acute pyelonephritis may begin explosively with chill, high fever, abdominal or flank pain, nausea, vomiting, urgent or burning urination. This syndrome may follow an upper respiratory infection, complicate the latter half of pregnancy, or supplement an attack of renal colic. It may follow diagnostic or therapeutic instrumentation or catheterization of the lower urinary tract. In older patients, particularly males with hypertrophied prostates, the onset may not be quite so dramatic, the temperature may be lower and the pain over the kidney region less severe. In severe infections chills and fever may recur daily or oftener with wide swings in temperature and drenching sweats on deferves-

tion of renal parenchyma is favored by the underlying obstructive lesions and later, the scars and deformities produced by the inflammation itself. Gradually, as more and more tubules are destroyed, replacement fibrosis occurs; this in turn strangles the preserved colloid-filled tubules. The glomeruli tend to hold out longer but ultimately succumb to the fibrosis around them. In addition, obliterative endarteritis adds to parenchymal ischemia and atrophy and may be associated with severe hypertension. This entire process may be uniformly distributed throughout both kidneys and lead to smooth shrinkage, or it may be focally expressed in chronic infiltrates and scars with intervening normal or hypertrophied parenchyma. Often, however, asymmetrical inflammation and atrophy occurs; in selected instances these may be responsible for a hypertensive syndrome including the malignant phase. Secondary hypertensive vascular changes may occur in the larger, better-functioning kidney. Pelvic and calyceal scarring with dilatation proximal to obstruction is responsible for pyelographic changes helpful in diagnosis.

*Symptoms and Course.*—Chronic pyelonephritis may run a variety of courses. Some patients, after a severe first attack, continue to have periods of low grade fever, general malaise, fatigue, unilateral or bilateral lumbar pain, gastrointestinal disturbance, mild secondary anemia, poor tolerance for exercise, and other nondescript symptoms. These may last for weeks or months, clear up and recur, often with some frequency or burning on urination. The urine may be grossly turbid or muddy and malodorous. Other patients go for months or years without subjective symptoms but occasionally experience a few days of fever and dysuria, with or without pain over one or both kidneys. The course may be completely asymptomatic for a long time except for some anemia and borderline rises in blood pressure. Prolonged and severe or accelerated hypertension may develop. In patients with kidney stones, attacks of colic and hematuria may precede recurrence of active symptoms of pyelonephritis and occasionally precipitate a fulminating infection with severe loin pain, chills, high fever, general toxemia and prostration. Acute pyonephrosis or multiple miliary abscesses are found in this condition, which is very dangerous when both kidneys are affected. In a small number of young subjects with unilateral atrophic pyelonephritis, a clinical syndrome develops with severe hypertension including the retinopathy of the malignant phase of hypertension, left ventricular hypertrophy and attacks of acute left-ventricular failure, severe tension headaches, dizziness, vomiting and even convulsive encephalopathy. Urinary tract infection may not be evident or suspected in this group until complete urographic and functional studies of each kidney are carried out. In chronic pyelonephritis the symptoms of an underlying obstructive lesion may confuse or dominate the picture.

In most patients with chronic pyelonephritis there is some degree of tubular impairment manifested by inability to concentrate the urine maximally. The urea nitrogen level of the blood may be little elevated in the earlier stages. Some hypochromic anemia is usually seen. Edema never occurs except as a sign of heart failure in the hypertensive patient or in the very late stages of the disease when uremia is already at hand. During the gradual development of renal insufficiency, considerable acidosis may supervene without affecting the patient remarkably apart from dyspnea on exertion. Occasionally the tubular impairment leads to a salt-losing disturbance which may mimic the dehydration and salt depletion of Addison's disease. In patients with calculous pyelonephritis secondary to hyperparathyroidism, the blood chemical and bony changes of the primary disease will be detectable, the former modified by renal insufficiency and its phosphate retention.

*Diagnosis.*—When the patient is first seen during an acute recurrence of chronic pyelonephritis, it may be difficult, without an adequate history, to distinguish it from an initial acute attack. Impaired renal function persisting after the acute symptoms have subsided speaks for the chronic renal involvement. Roentgen findings of irregularities, distortion, dilatation or constriction of renal pelves or calyces, often asym-

cultures of the urine are very helpful in some cases Also in acute glomerulonephritis which is usually produced by the beta hemolytic streptococcus, the antistreptolysin *titer in the serum will be high* Acute cystitis is usually distinguished from pyelonephritis by the frequency of urination, pain at beginning and end of urination, milder general symptoms and terminal hematuria Ordinarily, there is suprapubic or rectal tenderness but no lumbar tenderness Urinary casts are absent and the proteinuria is more in proportion to the hematuria and pyuria "Pyelitis" is not to be differentiated from what it really is—pyelonephritis

*Treatment* —The treatment of acute pyelonephritis begins with relief of any urinary-tract obstruction In children, the possibility of congenital strictures, valves aberrant renal vessels, malposition reduplication and other anomalies must be considered, *once the acute infection has been* brought under control

*Specific antibiotic treatment* will vary with the results of urine cultures While awaiting their outcome a combination of penicillin and sulfa or streptomycin or aureomycin, in full dosage is given for the first few days The sensitivity of urinary bacteria should be tested if there is any question about the clinical response Aureomycin or chloramphenicol may have to be used for relatively resistant gram negative bacilli To promote a high concentration of antibiotic in the urine, the fluid intake should not be forced too high early in the course unless there is considerable dehydration Treatment with antibiotics should be continued until pyuria has ceased and repeated urine cultures at intervals of several days or a week show no growth of the offending bacteria

*Symptomatic therapy* includes maintenance of adequate hydration prescription of a light diet (or parenteral feeding if necessary) the use of analgesics and sedation as indicated, the administration of supportive blood transfusions for anemia and good *nursing* during the recurrent chills, fever and sweats The bowels should be kept open with mild laxatives or small enemas Tympanites or ileus may require small doses of prostigmine Excessive vomiting may be *stopped by gastric intubation and aspiration* Careful replacement of fluids lost is necessary *to prevent dehydration and electrolyte im*balance This is particularly important in *children in whom the attack may begin with* diarrhea

Persistence or exacerbation of symptoms in spite of the preceding therapy, usually means obstruction or abscess formation somewhere in the upper urinary tract If this is located, temporary bypassing or other means of drainage may be required This is a specific urologic problem, and decision as to exact treatment should be arrived at through consultation Definitive surgery, such as nephrostomy, removal of stones, prostatectomy or nephrectomy, is post*poned until the acute infection has been* brought under control, if that is possible *However good surgical principles must be* followed in providing the necessary drainage *for renal or perinephritic collections of pus* When pyelonephritis complicates pregnancy, *ureteral catheter drainage may be necessary* for a period The antibiotics have changed the gravity of this combination and it is now hardly necessary to resort to termination of the pregnancy to relieve ureteral obstruction

## CHRONIC PYELONEPHRITIS

Chronic pyelonephritis is probably the most common chronic organic renal disease if one excludes hypertensive renal arteriolosclerosis It is often overlooked because of the insidious nature of its course in many cases and the long period it requires to produce renal insufficiency or other important signs A few cases first come to light because of a hypertensive syndrome associated with a predominant unilateral pyelonephritis of the atrophic variety In many cases uremia follows decades of smouldering or recurrent infection and gradual destruction and scarring of the kidneys For paraplegics and others with neurologic bladder disease chronic pyelonephritis still commonly shortens life

*Etiology and Pathogenesis* —The same pyogenic bacteria present in the urinary tract in acute pyelonephritis are *implicated* in the chronic process The repeated infec-

tion of renal parenchyma is favored by the underlying obstructive lesions and later the scars and deformities produced by the inflammation itself Gradually as more and more tubules are destroyed replacement fibrosis occurs this in turn strangles the preserved colloid filled tubules The glomeruli tend to hold out longer but ultimately succumb to the fibrosis around them In addition obliterative endarteritis adds to parenchymal ischemia and atrophy and may be associated with severe hypertension This entire process may be uniformly distributed throughout both kidneys and lead to smooth shrinkage or it may be focally expressed in chronic infiltrates and scars with intervening normal or hypertrophied parenchyma Often however asymmetrical inflammation and atrophy occurs in selected instances these may be responsible for a hypertensive syndrome including the malignant phase Secondary hypertensive vascular changes may occur in the larger, better-functioning kidney Pelvic and calyceal scarring with dilatation proximal to obstruction is responsible for pyelographic changes helpful in diagnosis

*Symptoms and Course* —Chronic pyelonephritis may run a variety of courses Some patients after a severe first attack continue to have periods of low grade fever general malaise fatigue unilateral or bilateral lumbar pain gastrointestinal disturbance mild secondary anemia poor tolerance for exercise and other nondescript symptoms These may last for weeks or months clear up and recur often with some frequency or burning on urination The urine may be grossly turbid or muddy and malodorous Other patients go for months or years without subjective symptoms but occasionally experience a few days of fever and dysuria with or without pain over one or both kidneys The course may be completely asymptomatic for a long time except for some anemia and borderline rises in blood pressure Prolonged and severe or accelerated hypertension may develop In patients with kidney stones attacks of colic and hematuria may precede recurrence of active symptoms of pyelonephritis and occasionally precipitate a fulminating infection with severe loin pain chills high fever general toxemia and prostration Acute pyonephrosis or multiple miliary abscesses are found in this condition, which is very dangerous when both kidneys are affected In a small number of young subjects with unilateral atrophic pyelonephritis a clinical syndrome develops with severe hypertension including the retinopathy of the malignant phase of hypertension left ventricular hypertrophy and attacks of acute left ventricular failure severe tension headaches dizziness vomiting and even convulsive encephalopathy Urinary tract infection may not be evident or suspected in this group until complete urographic and functional studies of each kidney are carried out In chronic pyelonephritis the symptoms of an underlying obstructive lesion may confuse or dominate the picture

In most patients with chronic pyelonephritis there is some degree of tubular impairment manifested by inability to concentrate the urine maximally The urea nitrogen level of the blood may be little elevated in the earlier stages Some hypochromic anemia is usually seen Edema never occurs except as a sign of heart failure in the hypertensive patient or in the very late stages of the disease when uremia is already at hand During the gradual development of renal insufficiency considerable acidosis may supervene without affecting the patient remarkably apart from dyspnea on exertion Occasionally the tubular impairment leads to a salt losing disturbance which may mimic the dehydration and salt depletion of Addison s disease In patients with calculous pyelonephritis secondary to hyperparathyroidism the blood chemical and bony changes of the primary disease will be detectable the former modified by renal insufficiency and its phosphate retention

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cultures of the urine are very helpful in some cases. Also, in acute glomerulonephritis which is usually produced by the beta-hemolytic streptococcus, the antistreptolysin titer in the serum will be high. Acute cystitis is usually distinguished from pyelonephritis by the frequency of urination, pain at beginning and end of urination, milder general symptoms and terminal hematuria. Ordinarily, there is suprapubic or rectal tenderness but no lumbar tenderness. Urinary casts are absent, and the proteinuria is more in proportion to the hematuria and pyuria. "Pyelitis" is not to be differentiated from what it really is—pyelonephritis.

*Treatment.*—The treatment of acute pyelonephritis begins with relief of any urinary-tract obstruction. In children, the possibility of congenital strictures, valves, aberrant renal vessels, malposition, reduplication and other anomalies must be considered once the acute infection has been brought under control.

*Specific antibiotic treatment* will vary with the results of urine cultures. While awaiting their outcome, a combination of penicillin and sulfa or streptomycin or aureomycin, in full dosage is given for the first few days. The sensitivity of urinary bacteria should be tested if there is any question about the clinical response. Aureomycin or chloramphenicol may have to be used for relatively resistant gram-negative bacilli. To promote a high concentration of antibiotic in the urine, the fluid intake should not be forced too high early in the course unless there is considerable dehydration. Treatment with antibiotics should be continued until pyuria has ceased and repeated urine cultures at intervals of several days or a week show no growth of the offending bacteria.

*Symptomatic therapy* includes maintenance of adequate hydration, prescription of a light diet (or parenteral feeding if necessary), the use of analgesics and sedation as indicated, the administration of supportive blood transfusions for anemia, and good nursing during the recurrent chills, fever and sweats. The bowels should be kept open with mild laxatives or small enemas. Tympanites or ileus may require small doses of prostigmine. Excessive vomiting may be stopped by gastric intubation and aspiration. Careful replacement of fluids lost is necessary to prevent dehydration and electrolyte imbalance. This is particularly important in children in whom the attack may begin with diarrhea.

Persistence or exacerbation of symptoms in spite of the preceding therapy, usually means obstruction or abscess formation somewhere in the upper urinary tract. If this is located, temporary by passing or other means of drainage may be required. This is a specific urologic problem, and decision as to exact treatment should be arrived at through consultation. Definitive surgery, such as nephrostomy, removal of stones, prostatectomy or nephrectomy, is postponed until the acute infection has been brought under control, if that is possible. However, good surgical principles must be followed in providing the necessary drainage for renal or perinephritic collections of pus. When pyelonephritis complicates pregnancy, ureteral catheter drainage may be necessary for a period. The antibiotics have changed the gravity of this combination, and it is now hardly necessary to resort to termination of the pregnancy to relieve ureteral obstruction.

## CHRONIC PYELONEPHRITIS

Chronic pyelonephritis is probably the most common chronic organic renal disease if one excludes hypertensive renal arteriolosclerosis. It is often overlooked because of the insidious nature of its course in many cases and the long period it requires to produce renal insufficiency or other important signs. A few cases first come to light because of a hypertensive syndrome associated with a predominant unilateral pyelonephritis of the atrophic variety. In many cases uremia follows decades of smouldering or recurrent infection and gradual destruction and scarring of the kidneys. For paraplegics and others with neurologic bladder disease chronic pyelonephritis still commonly shortens life.

*Etiology and Pathogenesis.*—The same pyogenic bacteria present in the urinary tract in acute pyelonephritis are implicated in the chronic process. The repeated infec

with the fluid intake increased to produce a larger urine volume There is no reason for restriction of salt Any febrile episode should be looked upon with suspicion as a possible index of recurrent renal infection Urine culture and examination of the urinary sediment and culture are indicated at such period

## TUBERCULOUS PYELONEPHRITIS

Tuberculous pyelonephritis is a prevalent and dangerous sequel to pulmonary tuberculosis or other source of hematogenous renal infection Because of its progressive and destructive course its ultimate extension to the urinary tract and the secondary involvement of the seminal vesicles the epididymis and the prostate as well as the risk of retrograde infection to the second kidney tuberculosis of the kidney must be diagnosed as early as possible It should be considered whenever a patient with any urinary tract symptoms and pyuria fails to respond to the usual treatment

*Etiology and Pathogenesis* —Tuberculous infection of the kidney begins with the formation of a tubercle around the bacilli in a terminal vessel of either the cortex or the medullary pyramid Caseation surrounding granulomatous inflammation and destruction of parenchyma proceed until the infection breaks through into the collecting ducts or ulcerates into one of the calyces of the renal pelvis Hemorrhage secondary infection cicatricial fibrosis and calcification occur in time Hydronephrosis and pyonephrosis may develop from ureteropelvic obstruction Rarely the ureter may be stenosed and the entire kidney closed off and rendered functionless though no longer a source of descending infection Tuberculous pyelonephritis may lead to an atrophic scarred and calcified kidney with considerable endarteritis This endarteritis may form a background for severe renal hypertension but it is amenable to nephrectomy in young patients The ulcerative changes in one or more calyces and the associated spasm or scarring furnish the basis for the diagnostic pyelographic findings In later stages the tuberculous cystitis at the ureteral orifice yields visual evidence during cystoscopy

*Symptoms and Course* —There may be no urinary-tract symptoms at the onset only the general manifestations of mild infection — malaise fatiguability slight fever night sweats weight loss and vague aches and pains More typically there are frequent and somewhat painful urination with bloody or cloudy urine variable renal or ureteral colic and at times attacks of acute pyelonephritis owing to mixed infection The suspicion of renal tuberculosis is sometimes aroused only by symptoms and signs of chronic epididymitis or prostatitis It is characteristic of uncomplicated renal tuberculosis that the urine is likely to be acid during pyuria and is sterile for ordinary pyogenic bacteria Albuminuria and turia are variable and not associated with casts Cultures of the concentrated sediment from 24-hour urines or samples obtained during urologic examination will often reveal acid fast bacilli Guinea-pig inoculation is necessary for absolute diagnosis Renal function and blood pressure are normal in the ordinary patient Renal insufficiency means extensive bilateral involvement *In nearly all* patients there will be definite *x* ray or other evidence of pulmonary tuberculosis or some other less common source of hematogenous renal infection

*In most patients with tuberculous pyelonephritis the course* is relentlessly progressive unless interrupted by treatment Apart from successive involvement of the lower urinary and genital tracts the possibility of secondary miliary spread via the circulation always threatens Suppurating fistulous tracts from infected urogenital structures add to the misery of the patient already plagued by severe bladder symptoms Amyloidosis may develop in these patients

*Diagnosis* —Evidence of previous pulmonary or bone tuberculosis or *x* ray or sputum findings of present infection are exceedingly important diagnostic aids Fine calcification focally in the renal *x* ray shadow is very suggestive of tuberculous pyelonephritis Careful and expert urologic studies urine cultures and guinea pig inoculation

metrical in the two kidneys, point to a chronic process. The presence of urolithiasis, ureteral stricture, prostatic hypertrophy, or urethral obstruction furnishes a diagnostic background for chronic urinary tract infection. The differential diagnosis from chronic glomerulonephritis is ordinarily easy. In the late pre-uremic stages of either disease the urine may not be helpful nor will any of the clinical findings be specific. If the history of the onset and course is not clearly available only retrograde pyelography may furnish the diagnostic clues to pyelonephritis. In patients over 50 chronic glomerulonephritis is less common than is pyelonephritis. Any demonstration of a significant urinary tract obstruction or anomaly of development should throw the balance heavily in favor of pyelonephritis. The differentiation from essential hypertension and hypertensive renal vascular disease usually offers no problem in cases with an adequate history. However difficulties in diagnosis may arise in the stage of severe renal insufficiency, when the blood pressure tends to rise, sometimes rapidly. Here a demonstration of the signs of prolonged hypertension—in the cardiac, cerebral, and retinal changes—should be possible in non-pyelonephritic cases. Small kidneys even without deformities of the pelves or calyces, suggest chronic pyelonephritis rather than hypertensive renal vascular disease. A family history of hypertensive disease may confuse the situation in a chronic pyelonephritic. Some clinicians believe that the hypertensive background is more important than the chronic renal infection in producing hypertension in these patients. The differential diagnosis of the malignant hypertension associated with unilateral atrophic pyelonephritis in children and young adults is exceedingly important. Some of these patients can be cured by nephrectomy. Hence every person with considerable hypertension who does not have a typical glomerulonephritis should undergo intravenous and if necessary retrograde pyelography. The question of the predominantly unilateral involvement by pyelonephritis or renal-vascular changes can only be settled by meticulous renal function studies of each kidney. Chronic pyelonephritis in pregnancy is usually distinguished from the hypertensive toxemias by the greater evidence of infection and the lesser effect on the blood pressure. Furthermore, edema is not part of the picture of pyelonephritis. Diabetic glomerulosclerosis may be confused with chronic pyelonephritis as a cause of renal disease in diabetics. Here the clinical presence of noncardiac edema and of doubly refractile lipoid cells and casts in the urine of patients with glomerulosclerosis is of great diagnostic value. The two conditions may be combined in diabetics toward the end of life.

*Prognosis.*—In the average adult case chronic pyelonephritis lasts for a few decades and then winds up in uremia or some hypertensive complication. The hazards of necessary surgical procedures also affect the prognosis, but the antibiotics have improved the outlook remarkably.

*Treatment.*—The best treatment for chronic pyelonephritis is *preventive*. This applies to the recognition and relief of urinary tract obstruction whenever feasible. The chemotherapy and antibiotic treatment of urinary infection is most important but can be carried out intelligently only after frequent urine cultures and sensitivity studies. Unfortunately the gram negative bacilli especially of the Aerobacter, Proteus and Pseudomonas group are likely to develop resistance to most of the sulfa drugs and antibiotics sooner or later. They should therefore be treated with full doses and for specific periods with interruption after several negative urine cultures. As long as calculi, large prostates, strictures or other obstructive lesions persist reinfection is inevitable. To this extent chronic pyelonephritis is a surgical disease and good urological surgery will act as a prophylactic. Foci of infection such as ulcerative colitis, decubital ulcers and other portals of entry of bacteria dangerous to the kidneys should be properly managed. General supportive measures, correction of anemia, bed rest during active renal infection and modification of diet as necessitated by severe renal insufficiency or hypertensive heart failure make up the *symptomatic therapy*. In the average case of chronic pyelonephritis the diet should be normal

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are indispensable for the diagnosis. The differential diagnosis includes urolithiasis, tumors, ordinary pyogenic pyelonephritis, nonspecific chronic cystitis or ureteritis, and atypical glomerulonephritis or glomerulitis. In rare cases, the diagnosis cannot be established until histologic studies are made of the removed kidney.

*Prognosis.*—The prognosis depends on early diagnosis, the individual's resistance, the maintenance of good nutrition and morale, adequate rest and time for healing and the control of spread of infection. The last can now be accomplished partly with the aid of streptomycin and other chemotherapy, but surgical removal of the grossly infected organ is usually still necessary. The antibiotics are of great value in clearing up residual sinuses and infected ureteral stumps.

*Treatment.*—Conservative early treatment of tuberculous pyelonephritis includes the proper use of streptomycin and often leads to the arresting or even healing of the smaller renal lesions associated with tubercle bacilluria.

In renal tuberculosis nephrectomy is indicated when there are diagnostic pyelographic changes and large ulcerating lesions. The pre- and postoperative periods should include streptomycin and p-amino-salicylic acid therapy. If the remaining kidney and lower urogenital tract are uninvolved, the patient may be considered cured but nevertheless should be trained to lead the life of an arrested case of tuberculosis. For complete security, urine cultures should be made frequently, even in the absence of symptoms.

## VASCULAR RENAL DISEASES

Vascular renal diseases include ordinary *hypertensive renal arterio and arteriolosclerosis*, diabetic glomerulosclerosis and the occlusive, inflammatory and allergic diseases of the kidneys.

## RENAL ARTERIAL OCCLUSION

Major renal arterial occlusion by arteriosclerotic thrombosis, embolism or inflammatory disease may be recognized when it occurs suddenly, by the development of renal pain, hematuria, hypertension at times, and evidence of loss of renal function on the affected side. In bilateral involvement, oliguria or anuria and uremia, usually with hypertensive features, appear quickly. Occlusion of small arterial branches with resulting small infarcts, may be easily overlooked unless the transitory gross or microscopic hematuria is detected. In the gradual involvement of one renal artery there may be no signs or symptoms of note if the other kidney is normal. Even accurate clearance tests will be difficult to interpret unless one thinks of the possibility of unilateral loss of renal function. Hypertension may result from unilateral renal arterial occlusion, pyelographic studies will detect unilateral failure of renal function. The presence of subacute bacterial endocarditis, acute myocardial infarction, auricular fibrillation, or other source of arterial embolism suggest major renal infarction. In case of septic emboli, renal suppuration will occur and produce the general symptoms of severe pyelonephritis.

*Treatment.*—Treatment is conservative and symptomatic. Nephrectomy is necessary for gross necrosis and suppuration and in the rare cases of Goldblatt hypertension diagnosed during life. In bilateral involvement, treatment is usually of no avail because of the irreversible uremia.

## RENAL VENOUS THROMBOSIS

Renal venous thrombosis may occur by extension from inflammation within the kidney, neoplastic invasion (as in hypernephromas) or extension of thrombosis from the inferior vena cava or as the result of the tendency to blood coagulation in certain diseases and cachectic states. There may be no obvious symptoms and only mild lumbar pain and only microscopic hematuria. On the other hand, renal venous thrombosis may begin with severe lumbar pain and tenderness, enlargement of the kidney and frank hematuria. When the disease is unilateral and gradual in occurrence a remarkable syndrome may result characterized by massive proteinuria, nephrotic edema and ascites, low serum albumin and hypercho-

lesterolemia even doubly refractile lipoid cells and casts may be found in the urine Renal function is usually impaired but not so seriously as one might expect Sudden bilateral occlusion of the renal veins usually causes death from uremia, often with hyper tensive symptoms

*Treatment* —Treatment is symptomatic to tide the patient over the period necessary for the development of collateral circulation Edema is managed as in chronic glomerulo nephritis and renal insufficiency in the usual manner

## ALLERGIC RENAL VASCULAR DISEASE

Allergic renal vascular disease includes the syndrome of periarteritis nodosa or polyarteritis the visceral lupus syndrome the visceral rheumatic purpuras and other affections of the arteries in infectious dis eases Unless hypertension edema urinary sediment changes and renal impairment are observed during the course of these diseases the renal vascular involvement will not be suspected Treatment is for the underlying condition and renal impairment if significant (For further discussion *see* section on Glomerulitis)

## ACUTE NECROTIZING TUBULAR NEPHROSES

Acute necrotizing tubular nephroses re sult from heavy metal and other inorganic and organic poisons of which mercury bis muth tartrates and carbon tetrachloride are representative from the hypoxic or ischemic necrosis following prolonged states of shock whether of hemorrhagic traumatic or infectious toxic origin from the degener ation and calcification due to endocrine and metabolic disturbances like hyperparathyroidism hypervitaminosis D or severe alkalosis from the tubular changes associated with acute hemolytic crises and from the intrarenal obstructive nephropathy ac companying precipitation of Bence Jones protein sulfa uric acid and other substances of poor solubility in the urine under certain conditions In general the tubular neph roses are acute and short lived due to rapid regeneration of tubular epithelium Once damage is severe enough to produce symptoms fatal oliguria and uremia are likely to ensue unless the patient can be tided over the few weeks required for restoration of anatomical tubular integrity

*Etiology and Pathogenesis* —The nephroses due to mercury bismuth uranium arsenic and other metallic poisons presumably result from direct precipitation or irreversible inactivation of important enzyme proteins in the tubular epithelium enzyme proteins that control the normal selective transfer mechanisms Glomerular filtration may still go on if the circulation is in good shape, but the filtrate entirely diffuses back through the damaged and necrotic proximal tubules Different chemical poisons may act maximally on the different segments of the proximal convoluted tubule but the net clinical result is essentially the same Even in the so-called lower nephron nephrosis associated with a large variety of conditions producing circulatory shock and renal hypoxia, the upper part of the nephron is probably not anatomically intact, nor is there good evidence that the severe renal dysfunction is chiefly of distal nephron origin In the nephroses characterized by the precipitation of blood pigment sulfa crystals Bence-Jones protein and other insoluble material in the lumen of the tubules, it is still uncertain how much this intrarenal obstruction interferes with kidney function The associated hemodynamic alterations and the interstitial inflammatory often granulomatous reaction in the kidney may be far more important in the clinical effect The nephroses occurring during severe alkalosis of pyloric or high intestinal obstruction or following excessive aspiration of gastric contents often cause much calcium deposition in necrotic or atrophic tubules Similarly acute exacerbations of hyperparathyroidism may lead to marked calcium infiltration of tubules and arterioles The nephroses produced by diethylene glycol or hypertonic sucrose cause striking hydropic swelling of proximal tubular epithelium, swelling sufficient to cause destruction of the lumen and probably cessation of filtration by increasing intracapsular pressure The attractive thesis that increased intrarenal

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precipitation in the urinary tract must be remembered If urine cannot be obtained and blood has not been drawn early enough the exact diagnosis may be difficult although the gravity of the renal disturbance will be obvious An *x* ray of the abdomen to exclude urolithiasis is often helpful Special tests are necessary to determine the etiology of paroxysmal hemoglobinurias and clinical hemolytic diseases

*Prognosis* —The prognosis varies with the degree of hemolysis the severity of the initial circulatory reaction the distribution of erythrocytic thrombi and emboli the nature of the underlying hemolytic disease or the gravity of the condition for which blood transfusion was given and the type of treatment given early and later A hemolytic nephrosis is always potentially fatal when severe oliguria or anuria is present However as long as even 50 or 100 cc of urine are excreted daily the outlook is not hopeless If the patient can be tided over the first 10 days and given time for tubular regeneration the prognosis improves rapidly Nearly all the deaths occur within the first two weeks

*Treatment* —Prevention is of paramount importance here at least with regard to incompatible blood transfusions Careful inquiry into previous transfusion experiences meticulous typing and subtyping of blood Rh typing and cross matching with free use of the Coombs test are worth the effort they require During blood transfusions close medical observation is imperative As a routine a sample of venous blood should be drawn at the end of each transfusion even when there is no reaction and immediately upon any suggestive symptoms Urine should be obtained before during and after each transfusion and carefully examined The urinary output of the patient should be recorded for at least 24 hours giving the volume and appearance of each specimen Blood transfusion of patients with hemolytic crises and severe anemia due to congenital defects or acquired hemolysins should be undertaken only after careful review of previous response to such treatment When the etiology of an attack of hemoglobinuria is known every effort should be made to prevent recurrent paroxysms by appropriate treatment of the etiological disease malaria or syphilis or the careful avoidance of exposure to cold strenuous muscular exercise (march hemoglobinuria) or the ingestion of the favus bean by susceptible persons

*Symptomatic treatment* of hemolytic nephrosis consists of the emergency management of the immediate circulatory shock with irradiated plasma or serum albumin and the later management of anuria and uremia Retyped and rematched blood may have to be given early or later for acutely dangerous anemia The use of hypertonic sodium bicarbonate or lactate solution intravenously as soon as the hemolysis is suspected may help prevent further precipitation of hemoglobin or its derivatives in the renal tubular lumen provided urine formation is still active Once urine flow is suppressed the administration of sodium salts simply aggravates the tendency to pulmonary and other edema and may cause dangerous alkalosis When diuresis returns specific electrolyte administration sufficient to offset urinary and extrarenal loss is necessary to prevent dangerous depletion and acidosis No diuretic drug is of value during hemolytic nephrosis and much harm may result from the use of such a drug However aminophyllin may be given for acute bronchospasm

## TRAUMATIC OR MYOGLOBIN NEPHROSIS

*Traumatic nephrosis* or crush syndrome accompanies crushing skeletal injuries involving muscle damage and circulatory shock It is a common result of the bombing of cities mining and other industrial accidents and automobile injuries It differs from other forms of acute ischemic nephrosis associated with prolonged shock in that myoglobin released from damaged muscle may precipitate as pigment casts in the lumen of renal tubules or appear in the urine like hemoglobin in hemolytic nephroses The exact toxic role of this pigment is still debatable

*Symptoms and Course* —The onset of oliguria and anuria following a crushing injury is often overlooked in the emergency

pressure due to edema is responsible for the anuria and uremia in most of the acute tubular nephropathies is not supported by sufficient physiological or therapeutic evidence. In practically all the nephroses in which the injurious factor acts only at one time or on a few occasions, the patient recovers from the original renal impairment or the general effects of the agent. Continuous or frequently repeated renal damage as a result of multiple myeloma, hyperparathyroidism or prolonged hypercalcemia of other origin causes foci of tubular atrophy, vascular damage, and interstitial fibrosis. These eventually combine to produce chronic irreversible renal disease.

## HEMOLYTIC NEPHROSIS

*Hemolytic, hemoglobinuric or blood-pigment nephrosis* is an important type of renal disease in these days of widespread use of blood transfusions. Apart from its etiology and certain special clinical features, its course and prognosis are quite similar to mercurial nephrosis (Chapter 13). It is included ordinarily among the so called lower nephron nephroses, but the upper nephron is probably severely affected functionally, if not anatomically.

*Etiology and Pathogenesis.*—Any acute hemolytic reaction, whether from incompatible blood transfusion, or any other cause may give rise to blood pigment nephrosis. The pathogenesis of the renal injury is now known to be much more complicated than was postulated by the original theory of simple obstruction of renal tubules by pigment casts. Pathological and experimental observations have led to the conclusion that the obstruction by pigment casts is relatively unimportant. Hemodynamic changes and renal hypoxia or anoxia are far more constant and significant findings. Direct toxic action of hemolyzed blood or of reabsorbed ferric iron on tubular epithelium may occur, too. Auxiliary factors like dehydration and strongly acid urine also play a role. The earliest change is marked renal ischemia and reduced glomerular filtration, soon followed by depression of tubular function. Secondary vascular thromboses and interstitial inflammation in the kidneys add to the functional disorganization. The general effects of circulatory collapse and the specific local effects of the etiological condition complicate the pathogenesis of the hemolytic nephroses.

*Symptoms and Course.*—The clinical picture varies with the underlying disturbance, but the renal syndrome is relatively uniform. The patient often first complains of lumbar pain or abdominal distress and may pass blood or reddish brown urine. Within a few hours, the urine output may fall to a very low level or cease entirely. Oppression in the chest, dyspnea, headache, vomiting, chill and fever, pains in the limbs and circulatory shock may occur in the more severe cases. There may be no obvious symptoms after a blood transfusion until anuria ensues. Slight to moderate icterus of the scleræ may be seen the day after the hemolytic episode but is often overlooked. The liver and spleen may become palpable and slight general edema may develop, especially if the patient continues to take food and fluids. The blood pressure may fall to shock levels in the initial reaction, if severe, but returns to the control value and later rises above normal as anuria continues. Severe anemia usually appears. Leukocytosis may be marked. The progression of asthenic uremia begins after a few days and takes its usual course to coma and death in from one to three weeks, unless urine flow is reestablished. Cerebral, cardiac or pulmonary manifestations from the original hemolytic disturbance will complicate the clinical picture.

*Diagnosis.*—The demonstration of hemoglobinuria with little or no hematuria and the finding of blood pigment casts is pathognomonic. If at the same time a blood sample is drawn very carefully to avoid hemolysis and free hemoglobin is seen in the serum, absolute confirmation is obtained. Since free hemoglobin is rapidly removed from the blood, the sample must be obtained immediately upon the suspicion of hemolysis. A few hours later the serum bilirubin will usually be elevated temporarily. The scleræ and skin later become icteric. Differentially, one must consider other red pigments in the urine, such as porphyrins, and hematuria of renal or lower urinary-tract origin. Sulfa

ureters usually lead to rapid improvement. Sulfa nephrosis results from direct toxicity of or allergic reaction to the drug and is not related to blood levels or urinary concentration. The kidneys may or may not show sulfa crystals in the tubular lumen or epithelium. They do show degeneration and necrosis of the nephrons, especially the distal nephrons, with considerable interstitial inflammation, arteritis and arteriolitis often granulomatous and edema. The glomeruli are also involved in the more severe cases. Lesions in other organs including the heart and the brain are not uncommon but may be difficult to diagnose clinically. The renal functional disorganization is the same as in other toxic nephroses; however, the kidneys may excrete urine in considerable amounts after infusion of isotonic saline, but with practically no sodium or chloride. The result is a remarkable elevation of the serum levels to as high as 180 meq. per liter for sodium and 150 meq. for chloride. This is usually associated with severe encephalitic symptoms and, unless early recognized and treated with nonsaline fluids, very likely to end fatally (Luetscher *et al.*).

## ALKALOTIC NEPHROSIS

Alkalotic nephrosis represents the late stages of severe renal damage produced by alkalosis, dehydration, cation deficits and other metabolic disturbances resulting from loss of upper gastrointestinal secretions, chiefly the gastric juice, by vomiting or tubal aspiration. This alkalosis in the past was often aggravated by administration of soluble alkali salts as antacids and the use of rigid Sippy diets in the milk and cream stage with their low sodium-chloride content. Refusal of food and fluids by the anorexic patient led to rapid azotemia in many instances. Nowadays, postoperative gastric suction to relieve distention and vomiting is a major cause of severe alkalosis.

*Etiology and Pathogenesis.*—When the gastric contents are lost for one reason or another, chloride leaves the body without its serum partner sodium. Bicarbonate, always available, expands to take the place of the lost chloride in extracellular fluids. This results in increased pH or alkalosis but is partly compensated for by higher excretion of sodium bicarbonate in an alkaline urine. However, as loss of upper gastrointestinal contents continues, not only hydrochloric acid but sodium chloride and water are lost and not replaced because of anorexia and poor intake or absence of salt in the dextrose solutions infused. Ultimately the serum sodium falls to levels of 120 milliequivalents or less in spite of increasing bicarbonate and decreasing chloride. At this point, dehydration and hemoconcentration have usually caused hemodynamic changes with deleterious effects on renal blood flow, glomerular filtration and tubular function. The kidney stops excreting sodium entirely, whether as bicarbonate or chloride, and one observes the paradox of an acid urine in the presence of severe internal alkalosis. Tubular degeneration, calcification and focal necrosis make their appearance and convert a functional into an organic renal disease with complete functional disorganization and rapid development of azotemia aggravated by toxic catabolism of protein. The process is reversible if recognized in time and runs the course of any other severe nephrosis except for the initial alkalosis. The alkalosis is gradually neutralized by uremic acidosis, the absence of anuria and the frequent depletion of potassium.

*Symptoms and Course.*—The alkalotic and renal symptoms often develop insidiously or are lost in the manifestations of heavy sedation, postoperative distress and cardiovascular and cerebral symptoms in the post hemorrhagic or postoperative states, especially in older age groups. Anorexia, nausea and vomiting, weakness, nervous irritability or apathy, confusional or delirious reactions, drowsiness or restless insomnia, stupor and twitchings (occasionally tetanic convulsions), respiratory difficulty and muscular paralysis (due to severe hypopotassemia)—any or all of these may occur. The patient usually shows considerable weight loss and signs of tissue dehydration. Muscular hyperesthesia is common. Hypotension and tachycardia are frequent. The urine output is often reduced to oliguric levels but there is seldom anuria. The urine is at first alka

of releasing the victim from the cause of the accident and in treating his shock. Characteristically, tremendous swelling of the injured limbs occurs after the crushing object or debris is removed. In the next few days, urinary output is insignificant and the clinical and chemical sings of asthenic uremia develop. The blood pressure may remain at low levels even after blood transfusion, and anemia replaces early hemoconcentration. The originally dark-reddish or chocolate-brown urine becomes lighter and its specific gravity isosthenuric in spite of the very small volume. Proteinuria, pigment and other casts, variable microscopic hematuria, and epithelial cells are found in the first urine the patient passes after the injury. Death occurs from uremia in most cases within a week or two even if the patient survives his original injuries. In the more fortunate group, urine flow is resumed gradually and after a diuretic phase with poor renal function, complete restitution occurs.

*Diagnosis.*—Diagnosis is easy whenever the urine is examined shortly after the crushing injury and before much blood has been transfused. After the treatment of shock the anuria may be confused with one arising from hemolysis. Spectroscopic analysis of the urinary pigment is required to differentiate myoglobin from hemoglobin derivatives.

*Treatment.*—Treatment consists in the management of traumatic shock, blood and plasma transfusion, compression bandaging of affected limbs to prevent massive swelling and sequestration of circulating volume into the crushed areas, early use of hypertonic sodium bicarbonate solution intravenously to keep the urine alkaline and prevent precipitation of myoglobin or metmyoglobin and prescription of a diet without protein or electrolytes but high in carbohydrate and fat, the administration of intravenous hypertonic glucose when indicated with restriction of fluids to the very minimum necessary for fluid balance. Known electrolyte losses by vomitus or otherwise are compensated. In short, this is the standard treatment for anuric nephrosis while awaiting tubular regeneration. Artificial dialysis is indicated under proper conditions.

## CARBON TETRACHLORIDE NEPHROSIS

Carbon tetrachloride nephrosis is associated with liver damage and gastrointestinal disturbance that often obscure the renal injury. After the initial anorexia, vomiting, abdominal distress, and early jaundice, symptoms of nervous irritability, stupor or confusion develop. Then oliguria becomes apparent and blood-chemical analyses disclose the usual signs of severe renal insufficiency. The urine, originally highly concentrated and deeply colored, becomes increasingly dilute and contains protein and bile-stained casts, with few erythrocytes unless there is a general bleeding tendency from low prothrombin level. The blood pressure may rise moderately during the anuric phase and some general edema appear if the patient has received considerable parenteral fluids. The course is like that of any other acute toxic nephrosis but is complicated by the effects of hepatic insufficiency aggravated by acute alcoholism. However, since the poisoning ordinarily occurs by inhalation of fumes under industrial conditions of exposure rather than by ingestion as in the experimental animal, hepatic damage is not so severe and recovery may occur without gross residual symptoms or signs. The treatment is the same as for any other anuric nephrosis, but for the sake of the liver, lipotropic agents, choline and methionine, should be administered early. High protein feeding is out of the question, although it is sometimes instituted by error before the renal lesion is recognized.

## SULFA NEPHROSIS

Sulfa nephrosis is fortunately a vanishing disease, thanks to the introduction of antibiotic drugs and greater care in the use of sulfa drugs. In its pathogenesis it is to be distinguished from the mere precipitation of sulfa compounds in the urinary passages, in this case discontinuing use of the drug, forcing fluids and early irrigation of the bladder and

ureters usually lead to rapid improvement Sulfa nephrosis results from direct toxicity of or allergic reaction to the drug and is not related to blood levels or urinary concentration The kidneys may or may not show sulfa crystals in the tubular lumen or epithelium They do show degeneration and necrosis of the nephrons especially the distal nephrons with considerable interstitial inflammation, arteritis and arteriolitis often granulomatous and edema The glomeruli are also involved in the more severe cases Lesions in other organs including the heart and the brain are not uncommon but may be difficult to diagnose clinically The renal functional disorganization is the same as in other toxic nephroses however the kidneys may excrete urine in considerable amounts after infusion of isotonic saline but with practically no sodium or chloride The result is a remarkable elevation of the serum levels to as high as 180 meq per liter for sodium and 150 meq for chloride This is usually associated with severe encephalitic symptoms and unless early recognized and treated with nonsaline fluids very likely to end fatally (Luetscher *et al*)

## ALKALOTIC NEPHROSIS

Alkalotic nephrosis represents the late stages of severe renal damage produced by alkalosis dehydration cation deficits and other metabolic disturbances resulting from loss of upper gastrointestinal secretions *chiefly the gastric juice by vomiting or tubal* aspiration This alkalosis in the past was often aggravated by administration of soluble alkali salts as antacids and the use of rigid Sippy diets in the milk and cream stage with their low sodium-chloride content Refusal of food and fluids by the anorexic patient led to rapid azotemia in many instances Nowadays postoperative gastric suction to relieve distention and vomiting is a major cause of severe alkalosis

*Etiology and Pathogenesis* —When the gastric contents are lost for one reason or another chloride leaves the body without its serum partner sodium Bicarbonate always available expands to take the place of the lost chloride in extracellular fluids This results in increased pH or alkalosis but is partly compensated for by higher excretion of sodium bicarbonate in an alkaline urine However, as loss of upper gastrointestinal contents continues not only hydrochloric acid but sodium chloride and water are lost and not replaced because of anorexia and poor intake or absence of salt in the dextrose solutions infused Ultimately the serum sodium falls to levels of 120 milliequivalents or less in spite of increasing bicarbonate and decreasing chloride At this point dehydration and hemoconcentration have usually caused hemodynamic changes with deleterious effects on renal blood flow glomerular filtration and tubular function The kidney stops excreting sodium entirely whether as bicarbonate or chloride, and one observes the paradox of an acid urine in the presence of severe internal alkalosis Tubular degeneration calcification and focal necrosis make their appearance and convert a functional into an organic renal disease with complete functional disorganization and rapid development of azotemia aggravated by toxic catabolism of protein The process is reversible if recognized in time and runs the course of any other severe nephrosis except for the initial alkalosis The alkalosis is gradually neutralized by uremic acidosis the absence of anuria and the frequent depletion of potassium

*Symptoms and Course* —The alkalotic and renal symptoms often develop insidiously or are lost in the manifestations of heavy sedation postoperative distress and cardiovascular and cerebral symptoms in the post hemorrhagic or postoperative states especially in older age groups Anorexia nausea and vomiting weakness nervous irritability or apathy confusional or delirious reactions drowsiness or restless insomnia stupor and twitchings (occasionally tetanic convulsions) respiratory difficulty and muscular paralysis (due to severe hypopotassemia)—any or all of these may occur The patient usually shows considerable weight loss and signs of tissue dehydration Muscular hyperesthesia is common Hypotension and tachycardia are frequent The urine output is often reduced to oliguric levels but there is seldom anuria The urine is at first alka

line but is later dilute and neutral or acid, showing only a small amount of protein and little or no cellular sediment The blood chemistry shows rapidly rising non protein and urea nitrogen, and creatinine level The non protein nitrogen varies with the amount of glucose and fluid given and retained The striking feature is the serum electrolyte pattern—sodium levels low chloride values reduced to 80—50 per cent of normal, and $CO_2$ or bicarbonate values doubled A low serum potassium level is common As uremic acidosis due to retention of sulfates, phosphates and organic acids sets in the serum bicarbonate level falls toward normal Hemoconcentration, low-plasma volume, and elevated plasma-protein values are observed These, however are modified by blood loss and protein depletion or by dilution of infused fluids The outcome in neglected cases is death in uremia or sudden cardiac or respiratory arrest attributable in some cases to potassium deficiency Proper treatment of severe alkalosis however regularly brings about dramatic and rapid improvement Renal function may not become entirely normal for months or never in the older patients Repeated reccurrence of milder episodes of alkalosis in peptic ulcer patients on very prolonged high daily intake of milk and alkaline antacids including calcium carbonate, may lead to the remarkable syndrome of nephrocalcinosis This is characterized by renal insufficiency hypercalcemia without hypophosphatemia or hypercalciuria and calcium deposits in the scleral conjunctiva and cornea where it can be readily detected by slit lamp examination (Burnett *et al* ) The condition represents a chronic alkalotic and hypercalcemic nephrosis with severe organic damage gradually or episodically produced

*Diagnosis* —Ordinary prerenal azotemia and organic uremias of various origins are readily distinguished from alkalotic nephrosis by their clinical background and the absence of chemical alkalosis Adrenal-cortical insufficiency must be considered but the low serum-bicarbonate level and the high serum potassium level and the presence of significant sodium and chloride concentrations in the urine usually distinguish such insufficiency from alkalotic nephrosis, even if other clinical data are not helpful

*Treatment —Prevention* of alkalotic nephrosis simply involves accurate recording of the volume of vomitus or gastric aspirate frequent checking up on the serum electrolytes especially chloride, bicarbonate, and sodium (the last is essential when the sum of the first two in milliequivalents is abnormally low) and eschewing the use of soluble alkalies as antacids Diet or administered fluids should contain enough sodium chloride to cover all possible losses and restore normal electrolyte balance in the serum Potassium deficits must be restored Food is the ideal vehicle for potassium but slow parenteral infusion of dilute potassium chloride (40 meq/liter) in Ringer s solution is indicated for patients who are vomiting Dehydration must be prevented by adequate fluids to maintain a urine volume of 1500 cc per 24 hours The urea nitrogen and creatinine levels of the blood are determined at frequent intervals Circulatory depletion and hypotension particularly after gastrointestinal bleeding or an operation, are best corrected with blood transfusions Any central nervous system symptoms should be considered possibly alkalotic or hypochloremic in origin until serum analyses prove otherwise Sedatives especially barbiturates and narcotics should not be given excessively if they are much confusion of the clinical picture results Bromides should never be used

*Symptomatic treatment* is essentially etiologic in this syndrome Since in most cases considerable dehydration accompanies the electrolyte loss isotonic saline solution or Ringer s solution with or without added potassium should be given parenterally Prolonged alkalosis severe renal damage persistent oliguria cardiac insufficiency and pulmonary congestion however often make it dangerous to administer over a short period the large volume of fluid necessary to carry in isotonic form the calculated deficit of sodium and chloride Here or when the dehydration is not serious it is quickest and safest to use a slow infusion of molar sodium-chloride solution About half the calculated deficit of salt in the extra

cellular fluids is given at one time and part of the rest later depending on the response of the patient and the results of serum analyses. Half molar ammonium-chloride solution given intravenously is also effective but furnishes no sodium and sometimes causes unpleasant reactions. Whenever the levels of both the serum sodium and the serum chloride are very low, hypertonic solutions of saline are mathematically indicated, as Peters has clearly shown. Only after major restoration of the serum-electrolyte pattern may isotonic solutions be given. Considerable urinary loss of potassium may occur during this restoration process, as well as decrease in the serum level associated with the disappearance of infused glucose from the blood stream. Symptomatic, electrocardiographic and chemical evidence of hypopotassemia should be carefully looked for and corrected. The attempt to lower azotemia by giving large amounts of fluid or intravenous glucose may produce the desired effect through diuresis but further aggravate electrolyte depletion. The diet—if the patient can eat—should at first be low in protein and high in carbohydrate and fat to reduce catabolism to the minimum. If parenteral feeding is necessary, glucose in a concentration of from 5 to 10 per cent is added to the electrolyte solutions. Adequate supplements of vitamins B and C are essential. Surgical relief of pyloric obstruction underlying the patient's alkalosis is deferred until the body fluid and electrolyte imbalance and renal function have improved considerably and the patient's general condition is suitable. This may take weeks of careful medical management.

## HYPERCALCEMIC NEPHROSES

Hypercalcemic nephrosis is found in association with acute or chronic hyperparathyroidism, acute or chronic vitamin D intoxication, rapid osteolytic metastases as a result of carcinoma of the breast (especially when aggravated by testosterone therapy) and in rare instances chronic peptic ulcer with hypercalcemia as a result of excessive ingestion of milk and alkalies containing calcium. The clinical syndrome is usually of an acute type and is often fatal.

*Pathogenesis.*—The pathogenesis of the disturbance is presumably tubular and vascular renal injury due to calcium precipitation. Other important factors are severe hemodynamic changes resulting from the general cardiovascular and neuromuscular effects of hypercalcemia and increased blood viscosity, dehydration from vomiting and anorexia, and the possible toxic action of protein derivatives released from bone matrix during rapid osteolysis. The result is severe renal impairment, oliguria and mounting retention of non protein nitrogen. A vicious cycle is established: the urinary calcium excretion is reduced from previously high levels and the hypercalcemia thereby aggravated. This may occur in spite of the rise in serum phosphate that accompanies the developing uremia. The renal process may end suddenly or gradually recede under treatment, presumably tubular regeneration occurs. But since hypercalcemia is often recurrent or chronic, the continued renal damage, both tubular and vascular, ultimately leads to atrophy of many tubules, interstitial fibrosis and increased calcification. In hyperparathyroidism gross nephrolithiasis is common; this is often complicated by calculous pyelonephritis and often ends in uremia. In other conditions the clinical and pathological data are insufficient to warrant discussion.

*Symptoms and Course.*—The symptoms of hypercalcemic nephrosis usually arise in the course of the underlying disease which may mask them. The most characteristic symptoms are rapidly developing anorexia, nausea, vomiting and acute abdominal pain. Nervous disturbances and marked muscular weakness are associated with symptoms of circulatory collapse. Vomitus and diarrheal stools may contain gross blood. Hemoconcentration may be striking and the blood very viscid or thin. Cyanosis occurs in the severe cases. The urine, at first concentrated and loaded with calcium compounds, is rapidly reduced in volume and becomes isosthenuric. It usually contains protein and often contains erythrocytes but is otherwise nonspecific. The blood's retention of nonprotein nitrogen is marked and the

serum-calcium levels are usually well above 12 mg per 100 cc Often the serum calcium levels rise acutely above previous high levels The inorganic phosphate level of the blood is either normal or elevated Other electrolyte disturbances are common, due to vomiting and diminished intake Circulatory collapse and uremia usually follow in severe or poorly treated cases In mild attacks recovery ensues with re-establishment of renal function and diuresis The pattern of renal dysfunction under an attack of hypercalcemic nephrosis is similar to that caused by any other acute toxic nephrosis but the exact steps in its development are not yet known Return to completely normal function may never occur in patients who otherwise recover Whether this indicates previous renal damage is not clear

*Diagnosis* —Striking gastrointestinal symptoms in a patient known or suspected of having a bone disease associated with hypercalcemia call for examination of the blood and the urine This should lead to a quick diagnosis A history of the patient s use of vitamin-D preparations for arthritis may reveal an important clue X-rays of the chest spinal column pelvis or skull may disclose osteolytic metastases in subjects not known to have primary malignant tumor One must of course consider other causes of abdominal pain and oliguria such as calculous obstruction acute pancreatitis or penetrating peptic ulcer intestinal obstruction Addison s disease and vascular accident No other type of toxic nephrosis is characterized by hypercalcemia

*Treatment* —Early diagnosis of the underlying disease and its appropriate treatment may prevent hypercalcemic nephrosis Hypercalcemia calls for prohibition of milk cheese other calcium foods vitamin D and testosterone and maintenance of a high fluid intake and urine volume There should be frequent check ups on the blood s calcium levels Special caution is indicated whenever a metastasis ridden patient is suddenly immobilized by a fracture or other disability At the slightest sign of gastrointestinal trouble or inability to drink the necessary amount of fluids parenteral hydration should be initiated

*Symptomatic treatment* consists in prompt dilution of the viscous blood by intravenous fluids, free from calcium and sufficient in daily amount to restore extrarenal losses as well as ensure a urinary output of at least 1,500 cc This is on the assumption that the kidney still responds to hydration Electrolyte imbalance or acidosis is corrected in the usual manner Glucose is given freely to reduce protein catabolism and the diet is kept free from protein until renal function improves Intravenous doses of sodium-citrate solution may be given cautiously in the hope of reducing the concentration of calcium ions especially in patients who do not immediately respond with diuresis and are in serious danger of continued calcium precipitation or cardiac damage After recovery patients should stick to the preventive regimen Resumption of testosterone or vitamin-D therapy is exceedingly dangerous In patients whose hyperparathyroidism is first diagnosed as the result of an attack of hypercalcemic nephrosis subsequent parathyroidectomy may be followed by a severe hypocalcemic tetany This requires vigorous calcium mobilizing treatment and the infusion of calcium compounds When hypercalcemic nephrosis occurs as part of a secondary or renal hyperparathyroidism treatment is effective only in so far as the chronically diseased kidneys can respond to the rehydration Since this complication is likely to be associated with a salt-losing type of renal insufficiency adequate intake of sodium preferably as sodium chloride to prevent an alkaline urine is necessary

## THE FUNCTIONAL RENAL DISEASES

The functional renal diseases include first the functional renal impairment of established hypertension with its general arteriolar vasoconstriction congestive heart failure constrictive pericarditis and the acute vascular toxemias of pregnancy second the hemodynamic disturbances associated with a multitude of insults to the body whether of hemolytic traumatic infectious toxic or metabolic origin (in this hemodynamic group the renal func

tional changes are only a brief step removed from the total disorganization resulting in the same kidneys once the organic nephrosis the so-called lower nephron nephrosis takes over in these two subdivisions of functional renal diseases the major etiological factor is *reduction in renal blood flow*) third renal dysfunctions attributable to imbalance of the hormones which normally influence the tubular reabsorption of water and electrolytes and to a lesser extent glucose and uric acid fourth disturbances attributable to such *inborn abnormalities* of renal enzyme pattern as renal diabetes the Fanconi syndrome renal rickets and osteomalacia and lack of capacity for ammonia production fifth *renal tubular enzymatic dysfunctions produced by drugs* (like phlorizine caronamide mercury and sulfanilamide) and dietary protein and sixth *renal venous congestion* or renal venous hypertension This is of vital importance in the common postural or orthostatic proteinuria and in certain phases of the edema of congestive heart failure

## RENAL DYSFUNCTIONS ASSOCIATED WITH RENAL ARTERIOLAR CONSTRICTION

The most important of these dysfunctions are circulatory *shock* acute and chronic *congestive heart failure* (including constrictive pericarditis) established vascular or *essential hypertension* and the acute vascular *toxemias of pregnancy* In all of these renal blood flow is more or less strikingly reduced Glomerular filtration is usually relatively less affected except in shock and in pregnancy Tubular function is variously affected it is normal in cases of early shock and in cases of chronic heart failure of rheumatic origin in younger patients is decreased in cases of hypertensive disease and is severely impaired in cases in the late stages of acute shock The same reduction in renal blood flow and rate of glomerular filtration may be found in both a severely edematous cardiac patient and a perfectly edema free hypertensive patient without heart failure Both may have normal venous pressure and normal plasma protein levels and be on the same salt intake Why the difference in renal excretion of salt? The renal tubules of the patient with heart failure probably are reabsorbing salt normally because presented with less than normal volume of filtrate the glomerulotubular imbalance favors the tubules In the hypertensive patient on the other hand the tubules are no longer normal can no longer normally dissociate salt from water and leak more salt under conditions of water diuresis There is no glomerulotubular imbalance and no edema develops for years in spite of the reduced rate of glomerular filtration Heart failure may of course supervene and further lower the filtration rate and upset the glomerulotubular balance Congestive heart failure is next to myocardial insufficiency a functional disease of the kidneys Functional renal disease is largely responsible for salt retention and cardiac edema Other factors hormonal and metabolic are also implicated in the complex syndrome of congestive heart failure but even some of these extrarenal factors may exercise much of their influence via the renal tubular reabsorptive mechanisms

To the extent that renal arterial and arteriolar constriction sets off tubular enzymatic processes that release vasopressor or vasotropic substances into the general circulation the toxemias of pregnancy are partly—at least in the early stages—renal functional disorders In time of course the organic glomerulonephrosis of pregnancy replaces the purely functional disturbance

The *symptoms* proceeding from renal arteriolar constriction depend on whether the process is acute or chronic and on what the underlying disease is In shock for example oliguria proteinuria concentration of the urine and striking reduction in renal blood flow and the rate of glomerular filtration are evident In chronic congestive heart failure the reduced rate of glomerular filtration and the glomerulotubular imbalance are important renal factors in both the retention of salt and water and the development of dyspnea edema hypervolemia and venous hypertension with their secondary hemodynamic consequences In the toxemias of pregnancy there is often a combination of hypertension edema and

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To the extent that renal arterial and arteriolar constriction sets off tubular enzymatic processes that release vasopressor or vasotropic substances into the general circulation, the toxemias of pregnancy are partly—at least in the early stages—renal functional disorders. In time, of course, the organic glomerulonephrosis of pregnancy replaces the purely functional disturbance.

The *symptoms* proceeding from renal arteriolar constriction depend on whether the process is acute or chronic and on what the underlying disease is. In shock, for example, oliguria, proteinuria, concentration of the urine and striking reduction in renal blood flow and the rate of glomerular filtration are evident. In chronic congestive heart failure the reduced rate of glomerular filtration and the glomerulotubular imbalance are important renal factors in both the retention of salt and water and the development of dyspnea, edema, hypervolemia and venous hypertension with their secondary hemodynamic consequences. In the toxemias of pregnancy there is often a combination of hypertension, edema and

proteinuria How much of the hypertension and the associated cerebral vascular reaction are renal in origin is not clear Nonprotein nitrogen retention occurs in the preceding conditions partly in accordance with reduced glomerular filtration rate which is not counterbalanced by extra intake of fluid to increase the urine volume on a given level of protein catabolism In patients with edema, it is difficult to achieve water diuresis unless salt is restricted

*Treatment* is to be directed toward the *etiologic disease* responsible for the renal hemodynamic alteration The renal dysfunction of shock, for example, is promptly alleviated by proper therapy for shock Restitution of circulating blood volume and lost extracellular fluids and electrolytes relieves the kidney of ischemia by increasing cardiac output and reduces the need for extreme tubular conservation of body water In cases of chronic heart failure, it may be practically impossible (which it is not in cases of acute heart failure) to increase materially the cardiac output the renal blood flow, and the rate of glomerular filtration The best way to deal with cardiac renal dysfunction, therefore is first to reduce the dietary salt intake so that less exogenous salt is retained and second to inhibit tubular reabsorption of salt by means of mercurial diuretics and auxiliary aids (ammonium chloride, aminophyllin) The latter favors the removal of edema fluid in spite of the reduced rate of glomerular filtration Measures that promote reabsorption of the edema fluid into the circulation—such measures as rest, elevation of the legs relief of abdominal or intrapleural pressure due to transudates, and digitalization—are helpful In the toxemias of pregnancy dietary control of sodium intake sedation to subdue excessive vasomotor stimulation and termination of pregnancy to correct the underlying hormonal imbalance are necessary to relieve the serious vascular disturbance of which the renal dysfunction is only one aspect

## HORMONAL RENAL TUBULAR DYSFUNCTIONS

*Diabetes Insipidus* —Diabetes insipidus manifests itself in renal symptoms striking polyuria with very dilute urine secondary thirst delayed response to sudden loads of water or electrolytes, and serum-electrolyte changes resulting from too much or too little sodium or chloride depending on the balance of intake and output

*Adrenal Cortical Disease* —Adrenal-cortical disease may affect renal function seriously either as a result of adrenal-cortical insufficiency (as in Addison s disease) or hyperadrenocorticism (as in the Cushing syndrome due to hyperplasia or neoplasia) It is to be noted that the therapeutic use of ACTH and cortisone may also affect renal function In Addison s disease renal dysfunction is a complex disturbance involving not only reduced blood flow and glomerular filtration but also (and more important) tubular impairment of reabsorption so severe as to bring about marked urinary loss *of sodium and chloride The electrolyte* depletion dehydration and hemoconcentration so produced may rapidly lead to circulatory collapse and accumulation on nonprotein nitrogen

*Cushing Syndrome* —In the Cushing syndrome, renal dysfunction occurs after the early stages filtration decreases the reabsorption of salt and water increases, this leading to diffuse edema Whether the hypertension is also of renal origin has not been determined

## HYPERPARATHYROIDISM

Hyperparathyroidism produces a functional renal disease owing to the action of the parathyroid hormone on tubular reabsorption (of phosphate primarily) the excretion of phosphate and calcium is increased This dysfunction sooner or later leads to calcium phosphate precipitation and to stone formation in the kidney In addition the effect of hypercalcemia on blood viscosity and circulation may produce acute depression of renal blood flow and filtration together with rapid development of azotemia The boundary line between this functional change and hypercalcemic nephrosis is tenuous The *symptoms* are those of the etiologic disease along with polyuria and high calcium *content in the* urine Abdominal pain oliguria nausea

and vomiting are serious danger signals of acute hyperparathyroidism and are soon followed by circulatory collapse and uremic stupor *Treatment* must concern itself with the primary condition in the parathyroids and with attempts to maintain a large urine volume to dilute the calcium and wash out non protein nitrogen and acid radicals

## ENZYMATIC RENAL TUBULAR DYSFUNCTIONS

*Renal Diabetes* —Renal diabetes is inherited The tubular reabsorption of glucose is less than normal and glycosuria occurs at blood-sugar levels below the usual threshhold The chief danger of the glycosuria lies in its being mistaken for the glycosuria of diabetes mellitus In renal diabetes the mechanism for the tubular reabsorption of glucose is impaired possibly because of inadequate phosphorylation the glucose Tm is reduced and rises in the blood glucose levels after meals or even during fasting lead to glycosuria If the glycosuria is severe ketosis may result particularly in children Restrictions of carbohydrates will favor the development of ketosis Mild cases of renal diabetes show no symptoms severe cases show the polyuria and thirst of glycosuria attacks of hypoglycemia and the secondary metabolic effects of lack of carbohydrates

*Treatment* consists in prescribing a diet high in carbohydrate to prevent hypoglycemia and ketosis Insulin is contraindicated There is no known method for increasing the tubular reabsorption of glucose to the normal level

*Fanconi Syndrome* —The Fanconi syndrome is a congenital renal dysfunction characterized by serious disturbance of growth severe rickets and bone deformities ketosis cystinuria and glycosuria There are striking changes in blood and urine The syndrome is due to a defect in the renal tubular reabsorption of phosphate amino acids calcium and glucose and often to impairment of ammonia production as well Organic acid excretion is greatly increased and acidosis results from loss of base Cystine may be deposited in various organs and cystine stones form in the urinary tract The full blown disease is usually seen in children who show severe and resistant rickets hypophosphatemia hypoglycemia, low serum levels of calcium sodium and bicarbonate elevated serum levels of chloride and very low serum levels of amino-acids In adults osteomalacia and the peculiar linear pseudofractures of Milkman s disease are associated with a similar renal defect in the reabsorption of phosphate and the inability to manufacture ammonia The enzymatic difficulty in the kidney is probably related to phosphorylation but the exact nature of the trouble is so far unknown

*Treatment* includes adequate nutrition to replace losses of glucose and amino acids, a high intake of calcium and phosphate and continued administration of sodium citrate or bicarbonate in amounts sufficient to prevent acidosis from urinary loss of base Alkalinization of the urine also prevents cystine precipitation High dosage of vitamin D may be necessary to cure the severe rickets Metabolic balance study is imperative for rational therapy

*Dietary Renal Dysfunction* —Many of the restricted dietary regimens used for renal diseases carry the implication that excess protein salt fat or other nutrient may, in time damage the function or structure of diseased kidneys But there is not good evidence to show that any balanced diet has a deleterious effect on diseased kidneys On the other hand it can readily be shown that glomerular and tubular clearances are reduced by diets low in salt or protein and increased by diets high in protein

*Hypertension of Renal Origin* —Hypertension of renal origin may be interpreted as an enzymatic tubular dysfunction if one believes in the formation and release of renin VEM and other vasoactive substances implicated in the theories of hypertension as resulting from some hypoxic disturbance in renal tubular metabolism On this basis the *treatment* of such hypertension should involve either increasing the oxygen supply or blood flow to the tubules or reducing their metabolic work to a degree compatible with their available oxygen supply The production of renal hyperemia for more than short periods is still an impractical if not unsafe

*proteinuria* How much of the hypertension and the associated cerebral vascular reaction are renal in origin is not clear Nonprotein nitrogen retention occurs in the preceding conditions partly in accordance with reduced glomerular filtration rate which is not counterbalanced by extra intake of fluid to increase the urine volume on a given level of protein catabolism In patients with edema, it is difficult to achieve water diuresis unless salt is restricted

*Treatment* is to be directed toward the *etiologic disease* responsible for the renal hemodynamic alteration The renal dysfunction of shock for example, is promptly alleviated by proper therapy for shock Restitution of circulating blood volume and lost extracellular fluids and electrolytes relieves the kidney of ischemia by increasing cardiac output and reduces the need for extreme tubular conservation of body water In cases of chronic heart failure it may be practically impossible (which it is not in cases of acute heart failure) to increase materially the cardiac output the renal blood flow, and the rate of glomerular filtration The best way to deal with cardiac renal dysfunction, therefore is first to reduce the dietary salt intake so that less exogenous salt is retained and second to inhibit tubular reabsorption of salt by means of mercurial diuretics and auxiliary aids (ammonium chloride aminophyllin) The latter favors the removal of edema fluid in spite of the reduced rate of glomerular filtration Measures that promote reabsorption of the edema fluid into the circulation—such measures as rest, elevation of the legs relief of abdominal or intrapleural pressure due to transudates and digitalization—are helpful In the toxemias of pregnancy dietary control of sodium intake sedation to subdue excessive vasomotor stimulation and termination of pregnancy to correct the underlying hormonal imbalance are necessary to relieve the serious vascular disturbance of which the renal dysfunction is only one aspect

## HORMONAL RENAL TUBULAR DYSFUNCTIONS

*Diabetes Insipidus* —Diabetes insipidus manifests itself in renal symptoms striking polyuria with very dilute urine, secondary thirst delayed response to sudden loads of water or electrolytes, and serum-electrolyte changes resulting from too much or too little sodium or chloride, depending on the balance of intake and output

*Adrenal Cortical Disease* —Adrenal-cortical disease may affect renal function seriously either as a result of adrenal-cortical insufficiency (as in Addison's disease) or hyperadrenocorticism (as in the Cushing syndrome due to hyperplasia or neoplasia) It is to be noted that the therapeutic use of ACTH and cortisone may also affect renal function In Addison's disease, renal dysfunction is a complex disturbance involving not only reduced blood flow and glomerular filtration but also (and more important) tubular impairment of reabsorption so severe as to bring about marked urinary loss of sodium and chloride The electrolyte depletion dehydration and hemoconcentration so produced may rapidly lead to circulatory collapse and accumulation on nonprotein nitrogen

*Cushing Syndrome* —In the Cushing syndrome renal dysfunction occurs after the early stages filtration decreases, the reabsorption of salt and water increases, this leading to diffuse edema Whether the hypertension is also of renal origin has not been determined

## HYPERPARATHYROIDISM

Hyperparathyroidism produces a functional renal disease owing to the action of the parathyroid hormone on tubular reabsorption (of phosphate primarily) the excretion of phosphate and calcium is increased This dysfunction sooner or later leads to calcium phosphate precipitation and to stone formation in the kidney In addition the effect of hypercalcemia on blood viscosity and circulation may produce acute depression of renal blood flow and filtration together with rapid development of azotemia The boundary line between this functional change and hypercalcemic nephrosis is tenuous The *symptoms* are those of the etiologic disease along with polyuria and high calcium content in the urine Abdominal pain oliguria nausea

an intravenous pyelogram should be made to exclude congenital renal anomalies, hydronephrosis or other lesions in which a postural increase of ordinarily slight proteinuria may be present.

*Treatment* involves complete reassurance of the patient or his parents as to the absence of organic renal disease.

*Cardiac Renal Dysfunction.*—Cardiac renal dysfunction is partly due to decreased renal blood flow secondary to diminished cardiac output and partly to renal venous congestion secondary to general venous hypertension. While acute rise in renal venous pressure of even moderate degree causes an acute reduction in urine volume and salt excretion, it is not established that persistent renal venous hypertension is an important factor in the salt retention and edema of chronic heart failure. It is difficult to prove this in heart failure, for both arterial inflow and venous outflow from the kidneys are abnormal. On the other hand, the edema associated with bilateral renal vein thrombosis is not a pure example either, because of the marked proteinuria and hypoproteinemia. The *treatment* of renal venous congestion in heart failure is obviously included in the management of heart failure *per se*.

## CONGENITAL MALFORMATIONS OF THE KIDNEYS

Anomalies of development of the kidneys are fairly common if minor variations are included. There are anomalies of position (malrotation or pelvic kidneys), of fusion (horseshoe kidney), of reduplication (double pelves or double kidneys), of vascular branching and course (producing constriction of the uretero-pelvic junction and hydronephrosis), of maturation of nephrons (giving rise to single or multiple cysts and the important variety of polycystic kidneys), of obstruction (due to stenosis, valves or neurologic anomalies). Complete agenesis or absence of one kidney may occur or marked hypoplasia on one side and compensatory hypertrophy of the other kidney. There may be bilateral hydronephrotic atrophy of the kidneys which is associated with idiopathic dilatation of the ureters and is commonly the background of renal dwarfism or renal rickets in late childhood or early adult life. Many of the anomalies involving hydronephrosis or atrophic kidney are sooner or later complicated by pyelonephritis.

## POLYCYSTIC KIDNEYS

Polycystic kidneys are, from the medical standpoint, the most important congenital disease of the kidneys because of the varied symptomatology, the long duration in many cases, the familial incidence and the diagnostic and therapeutic problems. While often associated with other anomalies of development, such as cysts in the liver or pancreas and cerebral vascular defects or aneurysms, the course of the disease is essentially dependent on the rate of development of renal insufficiency. This may be very slow and permit survival to the seventh decade or later.

*Etiology and Pathogenesis.*—Polycystic kidneys have a high familial incidence and are undoubtedly a hereditary anomaly. Careful study of the kidneys of lower vertebrates and mammals at different stages of development has led to the view that primitive tubules in the pronephric and mesonephric stages may fail to undergo complete atrophy in preparation for the later metanephros and that the continued secretion into the lumina of these blind tubules produces the cysts. Once cysts are formed, pressure atrophy of intervening normal nephrons gradually develops; this is compensated for by hypertrophy of the less affected nephrons. Distortions of vascular supply and lymphatic drainage, obstruction to urine flow down the collecting ducts or calyces and other difficulties are readily understood. Hemorrhage into cysts and infection or suppuration are common. The kidneys enlarged by the growth of innumerable cysts and hydronephrosis may reach enormous size (25 to 30 cm.) and weight (1 kilo each) and lead to abdominal distention and pressure on adjacent structures. Hypertension and renal insufficiency, usually without edema, are regular consequences. Death results from uremia or cardiovascular disease.

procedure The second alternative is the theoretical basis for the Kempner rice-diet treatment

*Drug Effects* —Drug effects on tubular functions are illustrated in the glycosuria produced by phlorhidzin which inhibits the tubular reabsorption of glucose in the salt- and water diuresis produced by organic mercurials in the phosphate and calcium diuresis caused by parathyroid hormone and in the caronamide inhibition of tubular excretion of penicillin The prevention of mercurial diuresis by BAL (dimercaptopropanol) is a striking example of protection of cellular enzymes by dithiol blocking of a heavy metal There are undoubtedly many other examples of drug induced functional renal disturbances including the self-depression of extraction by the tubules of diodrast p aminohippurate and phenol red by high blood levels of these compounds

## RENAL DYSFUNCTIONS DUE TO RENAL VENOUS CONGESTION

### Postural Proteinuria

Postural proteinuria or orthostatic albuminuria is the most important example of the role of venous congestion in producing a functional renal disease of major diagnostic significance This condition is found at some time or another in the majority of children especially during the rapid growth periods and in the early military ages However it may be observed even through the third and early fourth decade in persons with an asthenic build or poor posture The proteinuria is characteristically produced when the person stands up, especially if he is lordotic The albuminuria disappears when the patient lies down or is in the kyphotic posture The proteinuria almost entirely serum albuminuria, may vary from a trace to four plus although the total 24 hour loss rarely exceeds a few grams Hyaline and granular cylindruria and on occasion excess microscopic hematuria may occur Renal function blood pressure and general health are unimpaired even after years or decades of postural proteinuria The chief damage done by the disease is the anxiety created in the minds of the parents who are fearful of Bright s disease In adults the condition is a major nuisance when it is discovered during an insurance examination and leads to the rejection of the applicant

The *pathogenesis* of lordotic proteinuria has been variously ascribed to renal arterial or arteriolar constriction low pulse pressure and pressure of the lordotic spine on the left renal vein, which must cross over to the right However it has recently been clearly demonstrated by Bull that postural proteinuria is always lordotic in origin occurring even in the recumbent lordotic position and that it is bilateral and is regularly associated with a marked increase in venous pressure in the inferior vena cava below the liver—therefore also in the renal veins This venous congestion is apparently brought about by torsion of the liver on its axis with partial obstruction of the inferior vena cava, which is intimately related to its lower surface It can be reproduced by appropriate manipulation of the liver In addition to renal venous congestion renal blood flow, rate of glomerular filtration, urine volume and salt excretion, decrease sharply when the patient is in the abnormal posture

*Diagnosis* depends on establishing an exact relationship between the posture and the proteinuria Renal function tests and blood pressure should be entirely normal and the history negative for recent acute nephritis or pyelonephritis It may be difficult to obtain an entirely negative sample of urine even while the patient is lying down Nevertheless all specimens of urine must be obtained while the patient is in bed The striking increase in proteinuria during the active period of the day does not of itself distinguish this type of proteinuria from that of organic renal disease On the other hand the absence of protein red cells and casts in a highly concentrated night urine is of decisive diagnostic value The simplest office procedure is to give the subject a glass or two of water to provide urine during the test ask him to empty the bladder before and after 15 minutes of extreme lordosis then after 15 minutes of standing in kyphotic posture and again after 15 or 30 minutes of recumbency in kyphosis Only the first urine specimen should contain protein or formed elements In case of slightest doubt

struction in the abdomen complicates the situation Hypoproteinemia is rare in this disease Accurate renal clearances cannot be carried out because of the obstructive nature of the lesions The renal impairment is manifested in the usual urinary and blood-chemical changes and presents no specific pattern Hypertension is moderate in the earlier decades but later may achieve high levels of both systolic and diastolic pressure and in rare cases take on the aspect of malignant hypertension with all the typical cerebral retinal and cardiac manifestations Practically all adult patients with polycystic kidneys will show hypertension of some degree when the diagnosis is first made

*Diagnosis* —The association of hypertension urinary changes or any signs of renal impairment with palpable enlarged and often irregularly nodular kidneys at any age should warrant a strong suspicion of polycystic kidneys A family history of the disease is highly significant Certain diagnosis is achieved by means of intravenous or retrograde pyelography This will demonstrate the large kidneys the striking crescentic or arciform distortion and elongation of the calyces by the larger cysts and deformity or enlargement of the pelves Practically no other condition simulates this picture During an attack of hematuria in patients whose kidneys are not readily palpated the possibility of renal calculus tumor tuberculosis or nephritis must be considered and in these cases pyelography is the only way to make the diagnosis In patients with chills fever and pyuria the differential diagnosis of pyelonephritis and its background is involved At times bilateral hydronephrosis may be somewhat difficult to distinguish from polycystic kidneys Unilateral polycystic kidney may present a hard problem in diagnosis one that cannot be resolved except by surgical exploration Bilateral kidney tumors of malignant type especially in children may cause diagnostic confusion

*Treatment* —In the asymptomatic cases or those with only occasional hematuria no specific treatment is necessary until renal insufficiency or hypertensive symptoms become manifest Severe hematuria may require blood transfusions to counteract anemia Infections of the cysts are treated with antibiotics early, in the hope of preventing actual suppuration If there are signs of abscess formation exposure of the kidney and drainage of the particular cyst may be necessary Aspiration of accessible large cysts has been carried out with relief or pressure on the renal pelvis but this involves a definite risk when done without direct exposure of the kidney Surgical cauterization of the surface cysts is of value in special cases By and large however treatment should be conservative unless pelvic or ureteral obstruction, severe bleeding or suppurative infection results The hypertensive syndrome is managed largely from the standpoint of preventing cardiac failure or cerebral vascular strain Pregnancy should be discouraged in view of the hereditary nature of the disease However unless the kidneys are large enough to interfere with labor or considerable renal impairment exists there is no reason for terminating a pregnancy

## NEPHROLITHIASIS

Nephrolithiasis may affect any age group it is often associated with acute or chronic pyelonephritis

*Etiology and Pathogenesis* —The basic causes of precipitation of urinary solutes are still a matter of speculation but it is well established that in addition to the purely physicochemical factors of the solubility of calcium phosphate carbonate or oxalate magnesium phosphate uric acid and cystine supersaturation aided by various organic colloids in the urine and the tendency to precipitation of inorganic or organic solutes around a nidus of material (which may be necrotic tissue or a plaque in a renal papilla exudate blood clot foreign body) are etiologically important Once the initial precipitation occurs succeeding deposits of crystals may take place from supersaturated urine at appropriate pH The organic matrix of core of the calculus may begin in the kidney itself as a result of infection other inflammation or degeneration or develop in the lumen of a collecting duct from unknown causes Factors predisposing to stone formation are well known—metabolic

*Symptoms and Course* —If polycystic kidneys are large at birth, death may result from difficulties during delivery or shortly after from renal insufficiency In most cases, marked enlargement does not occur or is not detected for years There need be no symptoms whatsoever, and growth and development may be entirely normal A routine physical examination may reveal bilateral abdominal masses identifiable as Pregnancy or an abdominal operation may also reveal the presence of polycystic kidneys In some patients with such kidneys, the first "symptoms" may be unexplained anemia, weakness, hypertensive encephalopathy, or frank uremia

The *course* of the congenital disease usually lasts for four or five decades in patients fortunate enough to have had good renal function throughout childhood The

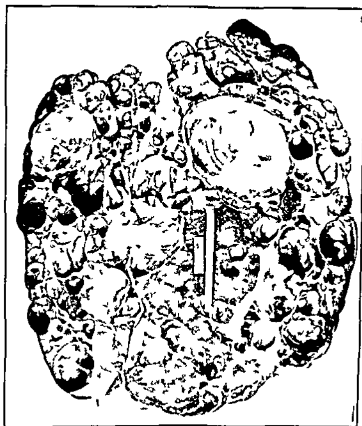


Fig 164



Fig 165

Fig 164 —Large polycystic kidney in sagittal section Note large areas of persisting parenchyma at the center and a few small areas elsewhere (Bell s Renal Diseases )

Fig 165 —Subclinical polycystic kidney Note large areas of persisting parenchyma This lesion did not cause uremia (Bell s Renal Diseases )

kidneys The young patient may come to the physician s attention because of an enlarged abdomen vague pains mild or severe hematuria renal colic without other signs of nephritis loin pain or chills and fever with or without pyuria In the older patient hypertension may be the first finding to lead to investigation of the kidneys Proteinuria is another sign that may first arouse suspicion of polycystic kidney course is often punctuated by attacks of pyelonephritis or suppuration in cysts and hemorrhages into the upper urinary tract with severe renal colic as blood clots are forced down the ureter These episodes may cause the patient considerable misery It is remarkable however how comfortable the patient may be for years despite very large kidneys Edema practically never occurs unless heart failure or venous ob

not developed The serum levels of calcium phosphate and phosphatase are normal unless the patient has parathyroid hyperfunction

*Diagnosis* —In any patient with lumbar pain renal colic proteinuria hematuria pyuria or general symptoms of urinary tract obstruction or infection nephrolithiasis must be seriously considered The same applies to attacks of abdominal pain nausea or vomiting or disturbance in bowel action not readily explained by specific gastrointestinal disease Patients suffering with paraplegia or acutely immobilized by fractures should be considered potential kidney stone patients In children with congenital metabolic disturbances in which cystinuria may occur kidney stones are likely to develop Renal insufficiency unexplained on other obvious grounds and osteoporosis or fibrocystic disease of bones should lead the physician to search for kidney stones With the exception of uric acid and cystine calculi kidney stones of significant size are radiopaque because of their calcium content Hence *x* ray studies preferably in the form of pyelography are most useful Differential diagnosis is chiefly concerned with distinction between kidney stones and other calcific shadows particularly gallstones and calcified mesenteric nodes or vascular lesions Careful analysis of the patient s history the physical and urinary findings and the *x* ray studies will usually clear up the situation The distinction between calculous disease of the kidneys and other renal diseases especially tuberculosis tumor or noncalculous pyelonephritis is ordinarily not difficult to make unless there are nonopaque or indefinitely outlined calculi Special diagnostic studies—cultures and inoculation of urinary sediment for tuberculosis and special staining of smears for neoplastic cells—prove helpful

*Treatment* —When a renal calculus is causing no trouble no specific treatment is necessary except for attempts to prevent further stone formation This *preventive* therapy however can be based intelligently only on a knowledge of the nature of the precipitated material Therefore a systematic chemical analysis should be made of any stone passed The type of stone can be determined with some accuracy from the density and morphological character of the calculus on the *x* ray films from the predisposing factors to stone formation in a given patient and from the finding of excess or abnormal crystals in freshly voided urines especially during periods of microscopic hematuria In the case of calcium phosphate or carbonate stones a high fluid intake and high urine volume (3 liters daily) must be maintained to reduce the calcium ion concentration At the same time the diet should be low in calcium especially in milk and cheese but high in vitamin A An acid urine (pH 5 2 to 5 4 and checked daily) should be maintained by an acid ash diet amplified by acid forming salts or ammonium mandelate For oxalate stones foods rich in oxalates (rhubarb beets spinach cocoa) should be restricted The urine should be kept slightly acid In the case of uric acid stones the opposite regimen—an alkaline ash diet moderately low in purine with alkalinizing salts to keep urates in solution—is employed Cystine is also held in solution by alkaline regimens In paraplegics and patients immobilized by casts or prolonged severe arthritis or ulcerative colitis with marked malnutrition frequent change of position to favor drainage from all parts of the renal pelves and close attention to diet and fluid intake to lower the calcium concentration and excretion in the urine are very important measures The same dietary regimen applies to patients exposed to subtropical desert climates that induce oliguria and large extrarenal losses of water Under these conditions renal calcium deposits have been observed to form within a matter of weeks if the diet and local water supply happened to be rich in calcium

The chief effects of nephrolithiasis are infection—pyelonephritis—and urinary tract obstruction (which in turn predispose to further stone formation by tissue destruction changes in urinary pH and production of stagnant urine saturated with poorly soluble crystalloids) these two sequela must be treated vigorously Unfortunately in the presence of stone and urinary obstruction infection is difficult to eradicate even with antibiotics and regularly recurs Resistant bacterial strains soon develop (*v*

disorders, such as cystinuria, oxaluria, gout or hyperparathyroidism, obstruction or stasis in the urinary tract and immobilization with its effects on the bones and the urinary calcium excretion as in paraplegics, low fluid intake and alkaline ash diets high in calcium and low in protein such as are common in tropical and subtropical regions, vitamin A deficiency with its metaplastic action on urinary tract epithelium and some sort of constitutional tendency to stone formation. The etiology of nephrolithiasis varies therefore with the type of stone found and is often complex.

Once the nucleus of a stone has developed in one or more sites in the kidney, the process goes on until the stone reaches a certain size at which it may then remain stationary for years. Local pressure atrophy of parenchyma and fibrosis occur but the major results are obstruction of some part of the calyceal system with dilatation proximal and soil favorable for infection or calculous pyelonephritis. Pressure erosion of local vessels often leads to bleeding. Pieces of a calculus may break away from the surface and pass on into the renal pelvis and ureter to produce colic, bleeding or obstruction, with or without infection. A stone originating in the pelvis may reach a large size with branching finger-like projections into the calyces—(the staghorn calculus). When the disease is bilateral sufficient destruction of parenchyma may result to produce severe renal insufficiency. Small stones may be passed repeatedly and new ones form over a period of years. In the case of uric acid calculi precipitates of urates may occur in masses throughout the pyramids and renal papillæ and give rise to the so-called uric acid infarcts.

*Symptoms and Course.*—The presence of nephrolithiasis may be entirely unsuspected for years. Sometimes incidental x-ray studies for gastrointestinal or vertebral column disease first reveal kidney stones; sometimes the finding of microscopic hematuria or pyuria during routine examinations first leads to an investigation of the urinary tract. Lumbar backache or abdominal distress at times precipitated or aggravated by activity associated with considerable jolting such as accompanies horseback riding or long motor trips over poor roads may be the presenting symptoms. The classical attack of acute renal colic is characterized by hematuria and vomiting or abdominal distention and constipation, and severe tenderness and spasm over the affected kidney or overlying abdominal wall. Symptoms of acute or chronic low grade pyelonephritis may be the only evidence of nephrolithiasis until x-ray and other urologic studies are made; recurrent gross hematuria may be the only symptom for years. Various gastrointestinal symptoms including the syndrome of spastic or irritable bowel, may lead the patient to one physician after another before the kidney stones are discovered. Patients with hyperparathyroidism may not be recognized as having either the primary parathyroid disease or the secondary nephrolithiasis till symptoms of the pre-uremic state appear. Nephrolithiasis may be associated with hypertensive disease, gouty arthritis, neurologic abnormalities and other conditions depending on the underlying or complicating disorder and the age of the patient.

The *urine* may be entirely negative but will usually show traces of proteinuria and microscopic hematuria. Excess leukocytes without casts will also usually be found in the urine. Crystals of the stone-forming material may be present in increased amounts but this is difficult to interpret unless substances like cystine, normally absent from the urine, are detected. Gross hematuria will occur during attacks of colic or even in pain-free intervals. The urine may be loaded with leukocytes and urea-splitting bacteria during periods of infection or as a persistent process when stones extend into the renal pelvis. The amount of protein in the urine is usually small, not more than one would expect from the quantity of blood in the sediment. The concentration of the urine may be entirely normal in many cases but will reflect renal impairment or obstruction in others. In about half the cases of calcium stones the Sulkowitch test usually reveals excessive calcium concentration in the urine even when the diet is low in calcium.

The *blood chemistry* is usually not altered in nephrolithiasis if renal impairment has

and hemorrhage followed by cholesterol and calcium precipitation are very frequent in malignant renal tumors and give rise to irregular or continuous fever leukocytosis and other general symptoms The neurogenic tumors metastasize readily into the liver the lungs and remarkably the cranial bones of the orbital wall in children Displacement of abdominal organs and distortions of the pelvis and ureter are common results of large renal tumors

*Symptoms and Course*—Even tumors of some size may be asymptomatic in the renal cortex Symptoms arise when the tumor reaches the pelvis and bleeds ulcerates or causes local obstruction Ordinarily painless hematuria is an early symptom This may be slight or massive intermittent or continuous Dull pain in the flank pain *often radiating into the abdomen may* appear early or late A mass is often palpable especially in the more accessible right kidney Low intermittent fever or prolonged pyrexia is seen in patients with urinary tract infection or large tumors undergoing necrosis Hemorrhage into the perirenal tissues may give rise to acute abdominal pain vomiting and other signs of peritoneal irritation The patient may have no obvious renal symptoms but general malaise fatiguability weight loss anemia moderate leukocytosis and an elevated erythrocyte-sedimentation rate In some patients the first symptom of a hypernephroma may be a varicocele or hydrocele due to invasion by tumor or thrombosis of the spermatic vein especially on the left In others pathological fracture of a long bone or accidental *x* ray demonstration of an osteolytic lesion in the skull or a pulmonary metastasis first suggests renal carcinoma Symptoms of cerebral metastasis may also give the first clue In children enlargement of the abdomen is an important sign of rapidly growing tumors The kidney may or may not be tender or enlarged in patients with renal tumors Obviously the small tumors will produce no local physical signs The larger growths may reflect themselves in hydronephrotic or irregular nodular kidneys mobile or fixed In advanced cases of malignancy both kidneys may be involved and signs of occlusion of the inferior vena cava—edema of the legs scrotum and lower back collateral veins hemorrhoids—may be prominent In these cases chemical evidence of renal impairment can be elicited

The urine may be normal in cases of parenchymal renal tumor of small size Ordinarily, hematuria of varying degree pyuria (in case of secondary infection or ulceration) albuminuria not disproportional to the bleeding (except when the renal vein is thrombosed) and in a limited number of cases conglomerates of tumor cells in the urinary sediment may be expected The cystoscopic and urographic examinations will demonstrate unilateral bleeding and renal pelvic abnormalities in the form of caliceal distortion elongation or obliteration filling defects hydronephrosis or enlargement of the affected kidney Perirenal hemorrhage *may obliterate the iliopsoas muscle s shadow* In some early cases even after careful and repeated *x* ray studies to explain the unilateral hematuria nothing abnormal can be found and only surgical exploration of the kidney will disclose the tumor

*Prognosis*—The prognosis varies with the type of malignant tumor the time of its recognition and the presence or absence of venous invasion or metastases About 20 per cent of nephrectomized adult patients survive 5 years The outlook for children with rapidly growing embryonal tumors is much less hopeful

*Diagnosis*—The chief diagnostic problem is simply recognizing the presence of renal tumor The differential diagnosis therefore concerns the numerous causes of hematuria In the absence of urinary or general clinical signs of bilateral renal disease or blood dyscrasia prompt cystoscopic and urographic examinations are indicated Renal tuberculosis must be ruled out if the tumor is not large enough to produce typical *x* ray findings Nonopaque calculi may create confusion in the absence of attacks of renal colic In all cases suspected of renal tumor the chest and skull also should be *x* rayed Patients with brain tumors may be suffering from metastases from primary renal malignancy Patients with unexplained fever weight loss and anemia who are in the high frequency decades for cancer should be given urologic diagnostic study

"Pyelonephritis") The urea-splitting organisms (e g, staphylococci and B proteus) are a particularly tough problem, for the alkaline reaction they cause strongly favors calcium and magnesium precipitation Obviously the vicious circle can only be broken by surgical therapy of the nephrolithiasis The stone may be removed, a portion of the kidney resected or complete nephrectomy carried out In recent years, there has been a strong tendency to preserve as much of the kidney as possible by appropriate plastic procedures If the kidney stones are secondary to parathyroid tumor or hyperplasia the surgical treatment should be directed early to the parathyroid in order to stop the hypercalcemia and the continued precipitation of calcium salts in the kidney If large or multiple renal calculi extend into the pelvis or surgery is contraindicated because of bilateral renal involvement renal insufficiency or the patient's general condition the use of irrigating solutions via ureteral catheter or nephrostomy tube may be tried This procedure has been successful in enough cases to warrant further trial under careful urologic control The solutions vary in composition but generally contain citric acid magnesium citrate and sodium carbonate and yield a pH of 4 2 (tolerated by the mucosa of the urinary tract)

## RENAL NEOPLASMS

Neoplasms of the kidney include a variety of benign and malignant tumors the latter generally occurring in persons over 40 though the neurogenic tumors and the highly malignant embryonal adenomyosarcoma (Wilms tumor) are found in infants and young children Painless hematuria is a common symptom but the clinical picture varies with the location the rate of growth and the nature of the extension of the tumor

*Classification* —Renal neoplasms originate in the parenchyma in 80 or 85 per cent of the cases and in the pelvis in about 15 per cent Neoplasms rarely originate in the capsule of the kidney The *parenchymal* tumors are, with few exceptions malignant the majority being carcinomas (hypernephromas or Grawitz tumors) of the alveolar papillary, or tubular variety Papillary cystadenomas or carcinomas also occur either singly or in multiple form in fibrotic kidneys Highly malignant mixed tumors or carcinosarcomas occur in adults Wilms tumor is the counterpart in infants True adrenal rest tumors are very rare but when found, are usually located near the capsule

*Tumors of the renal pelvis* are either papillary or epidermoid and are of the squamous-cell type If epidermoid they are often associated with calculus or with epithelial tumors in the lower urinary tract

*Tumors of the renal capsule* usually consist of lipomas fibromas or corresponding sarcomas

*Etiology and Pathogenesis* —The incidence of renal neoplasms is more than twice as high in males as it is in females Though the most common malignant renal neoplasms in adults the hypernephromas were originally believed to originate in adrenal-cortical rests these tumors are now known to arise from renal tubular epithelium The adenomyosarcomas of children are considered to be either teratomatous or embryonal nephrogenic in origin No known urinary constituent has ever been shown to be neoplastogenic but one must remember the continuous excretion of a host of steroid compounds of hormonal and other metabolic origin There is no evidence of an industrial origin for kidney tumors as there is for bladder tumors among aniline dye workers A renal neoplasm may exert pressure on surrounding renal tissue or a calyx and cause local obstruction Invasion of veins by hypernephromas and other renal tumors is very common and leads to thrombosis hemorrhage and necrosis as well as to eventual metastases of the lungs bones and other structures If the tumor breaks into the pelvis ulceration bleeding obstruction and infection soon occur and may present the first gross signs of disease Invasion of the kidney capsule and perinephric fat is a late stage of malignant renal tumors The adrenal gland may be surrounded by the tumor mass Renal venous tumor thrombosis may cause infarction of the kidney or extend into the inferior vena cava and the opposite renal vein to produce the usual signs of major venous obstruction Necrosis

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the hope being that operable renal tumors may be detected In children suspected of having Wilms tumor preoperative radio therapy may lead to rapid decrease in the size of the tumor and furnish a diagnostic aid Lymphoblastomatous infiltration of the kidneys may cause confusion in diagnosis but such infiltration is usually bilateral and rarely produces renal symptoms without other clinical signs of lymphomatous disease Renal bleeding due to varices in the pelvis or other vascular lesions may cause considerable difficulty in differential diagnosis, especially when clots in the pelvis produce filling defects Repeated examination is of value in case of doubt exploration alone is certain

*Treatment* —Treatment of renal neoplasms is surgical Radiotherapy may be a useful adjunct however in the management of certain embryonal tumors in children and in lymphomatous involvement of the kidneys

BIBLIOGRAPHY


ADDIS T Glomerular Nephritis Diagnosis and Treatment New York MacMillan 1948

ADDIS T and OLIVER J The Renal Lesion in Bright s Disease New York Paul B Hoeber 1931

ALBRIGHT F DRAKE T G and SULKOWITCH H W Renal Osteitis Fibrosa Cystica Bull John Hopkins Hosp 1937 *60* 377

BARNES L A MOLL G H and JANEWAY C A Nephrotic Syndrome I Natural History of the Disease Pediatrics 1950 *5* 486

BELL E T Renal Diseases 2nd Edition Philadelphia Lea & Febiger 1950

BLACKMAN S S JR GOODWIN W E and BUELL M V Concentration of Total Protein and Globulin in Urine and the Pathogenesis of Renal Lesions Bull Johns Hopkins Hosp 1941 *69* 397

BLAKE W D *et al* Effect of Increased Renal Venous Pressure on Renal Function Am J Physiol 1949 *157* 1

BRADLEY S E and TYSON C J Nephrotic Syndrome New England J Med 1948 *38* 223 and 260

BRIGHT R Cases and Observations on Renal Disease Accompanied by the Secretion of Albuminous Urine Guy s Hosp Report 1836 *1* 338

BULL G M Postural Proteinuria Clin Science 1948 *7* 77

BURNETT C H *et al* Renal Function Studies in the Wounded Surgery 1947 *22* 856 and 981

— — Hypercalcemia Without Hypercalcuria or Hypophosphatemia Calcinosis and Renal Insufficiency New England J Med 1949 *240* 787

CAVELTI P A Pathogenesis of Glomerulonephritis and Rheumatic Fever Arch Path 1947 *44* 119

CHAPMAN C B and GIBBONS T B The Diet and Hypertension Medicine 1949 *29* 29

CHASIS H GOLDRING W and BALDWIN D S The Effect of Nitrogen Mustard on Renal Manifestations of Human Glomerulonephritis J Clin Investigation 1950 *29* Proceeding

CORCORAN A C TAYLOR R D and PAGE I H Functional Patterns in Renal Disease Ann Int Med 1948 *28* 560

DARROW D C Disturbances in Electrolyte Metabolism in Man and their Management Bull N Y Acad Med 1948 *24* 147

EARLE D P JR Renal Function Tests in the Diagnosis of Glomerular and Tubular Disease Bull N Y Acad Med 1950 *26* 47

FARR L E and MACFAYDEN D A Hypoaminoacidemia in Children with Nephrotic Crises Am J Dis Child 1940 *59* 782

FISHBERG A M Hypertension and Nephritis 4th Ed Philadelphia Lea & Febiger 1944

FOX C L JR and MCCUNE D J Electrolyte Changes in Nephrosis Am J Med Sci 1948 *216* 1

GOLDBLATT H The Renal Origin of Hypertension Physiol Rev 1947 *27* 120

GOLDRING W and CHASIS H Hypertension and Hypertensive Disease New York The Commonwealth Fund 1944

GREENSPAN E M Hyperchloremic Acidosis and Hypercalcinosis The Syndrome of Pure Lower Nephron Insufficiency Arch Int Med 1949 *83* 271

GROLLMAN A MUIRHEAD E E and VANATTA J Rôle of the Kidney in Pathogenesis of Hypertension as Determined by Effects of Bilateral Nephrectomy Am J Physiol 1949 *157* 21

HARRISON T R and MASON M F Pathogenesis of Uremic Syndrome Medicine 1947 *16* 1

HERMANN J B KIRSTEN F and KRAKAUER J S Hypercalcemic Syndrome Associated with Androgenic and Estrogenic Therapy J Clin Endocrin 1949 *9* 1

HIGGINS C C Renal Lithiasis J Urol 1949 *? * 403

JANEWAY C A HUTCHINS G *et al* Diuresis in Children With Nephrosis Response to Measles Tr A Am Physicians 1948 *61* 108

KEMPNER W Compensation of Renal Metabolic Dysfunction Treatment of Kidney Disease and Hypertensive Vascular Disease with a Rice Diet North Carolina Med J 1945 *6* 117

KIMMELSTIEL P and WILSON C Intercapillary Lesions in the Glomeruli of the Kidney Am J Path 1936 *12* 83

LAUSON H D BRADLEY S E and COURNAND A The Renal Circulation in Shock J Clin Investigation 1944 *23* 381

LEITER L Renal Diseases Some Facts and Problems Ann Int Med 1948 *28* 229

— Nephrosis Medicine 1931 *10* 135

LONGCOPE W T and LUETSCHER J A JR The Use of BAL in the Treatment of the Injurious Effects of Arsenic Mercury and other Metallic Poisons Ann Int Med 1949 31 545

LONGCOPE W T O'BRIEN D P McGUIRE J HANSEN O C and DENNY E R Relationship of Acute Infections to Glomerular Nephritis Jr Clin Investigation 1927 5 7

LONGCOPE W T and WINKENWERDER W L Clinical Features of the Contracted Kidney due to Pyelonephritis Bull Johns Hopkins Hosp 1133 53 255

LUCKE B Lower Nephron Nephrosis (Renal Lesions of Crush Syndrome of Burns Transfusions and Other Conditions Affecting Lower Segments of Nephron) Mil Surgeon 1946 99 371

LUETSCHER J A JR HALL A D and KREMER V L Treatment of Nephrosis with Concentrated Human Serum Albumin I Effects on the Proteins of Body Fluid J Clin Investigation 1949 28 700

LUETSCHER J A JR and BLACKMAN S S JR Severe Injury to Kidneys and Brain Following Sulfathiazole Administration High Serum Sodium and Chloride Levels Ann Int Med 1943 18 741

MASUGI M Über die experimentelle Glomerulonephritis durch das Spezifische Antinierenserum Ein Beitrag zur Pathogenese der diffusen Glomerulonephritis Beitr z path Anat u z allg Path 1934 92 429

McCUNE D J MASON H H and CLARKE H T Intractable Hypophosphatemic Rickets with Renal Glycosuria and Acidosis (The Fanconi Syndrome) Am J Dis Child 1943 65 81

MELICOW M M Classification of Renal Neoplasms J Urol 1944 51 333

MERRILL A J Edema and Decreased Renal Blood Flow in Patients with Chronic Congestive Heart Failure J Clin Investigation 1946 25 389

OLIVER J New Directions in Renal Morphology The Method its Results and its Future Harvey Lectures 1944 40 102

——— The Structure of Metabolic Process in the Nephron J Mt Sinai Hosp 1948 15 175

PETERS J P Salt and Water Metabolism in Nephritis Medicine 1932 11 435

RAASCHOU F Studies of Chronic Pyelonephritis Copenhagen E Munksgaard 1948

RIFKIN H et al Diabetic Glomerulosclerosis Clinical and Pathological Observation Doubly Refractile Fatty Cells and Casts in the Urine Medicine 1948 27 429

RUDEBECK J Clinical and Prognostic Aspects of Acute Nephritis Acta med Scandinav Supp 173 1946

RYTAND D Fatal Anuria The Nephrotic Syndrome and Glomerular Nephritis as Sequels of the Dermatitis of Poison Oak Am J Med 1948 5 548

SELYE H General Adaptation Syndrome and Diseases of Adaptation Jr Clin Endocrinol 1946 6 117

SHORR E ZWEIFACH B W et al Hepato-renal Vasotropic Factors in Experimental Shock and Hypertension Tr A Am Physicians 1947 60 28

SIROTA J H Carbon Tetrachloride Poisoning in Man the Mechanism of Renal Failure and Recovery J Clin Investigation 1949 28 1412

SMADEL J F Experimental Nephritis in Rats Induced by Injection of Anti Kidney Serum J Exper Med 1936 64 921 1937 65 541

SMITH H W Studies in the Physiology of the Kidney (Porter Lectures) Lawrence Kans Univ of Kansas 1943

——— The Excretion of Water Bull N Y Acad Med 1947 23 177

SNAPPER I Management of Acute Renal Failure Bull N Y Acad Med 1949 25 199

STERNHEIMER R and MALBIN B I A New Stain for Urinary Sediments Its value in the Differential Diagnosis of Hypertension Am Heart J 1949 37 678

VANATTA J MUIRHEAD E E and GROLLMAN A Improvements on the Artificial Kidney An Experimental Study of its Applications Am J Physiol 1949 156 443

VAN SLYKE D D The Effects of Shock on the Kidney Ann Int Med 1948 28 701

VAN SLYKE D D et al Observations on the Courses of Different Types of Bright's Disease and on the Resultant Changes in Renal Anatomy Medicine 1930 9 257

VAN SLYKE K K and EVANS E I The Paradox of Aciduria in Hypochloremic Alkalosis Ann Surg 1947 126 545

VOLHARD F Nieren und ableitende Harnwege in Handb d inn Med Bd VI Teil I u II Berlin Bergmann and Staehelin II Aufl Springer 1931

VOLHARD F and FAHR T Die Brightsche Nierenkrankheit Berlin Julius Springer 1914

WEISS S and PARKER F JR Pyelonephritis Its Relation to Vascular Lesions and to Arterial Hypertension Medicine 1939 18 221

WESTON R E et al Pathogenesis and Treatment of Salt and Water Retention in Congestive Failure Med Clin N Am 1950 34 615

WHITE J C Nephrosis Occurring During Trimethadione Therapy J A M A 1949 139 376

WOHL M G and ROBERTSON H E Nonrenal (Extrarenal) Azotemia Med Clinics North America November 1940

WOHL M G BRUST and R W FREED H Nonrenal Azotemia J Lab and Clin Med 1938 23 450

Chapter

# 24

# Diseases of Blood Vessels and Lymph Vessels and Abnormalities of Blood Pressure

By IRVING SHERWOOD WRIGHT M D and CHARLES D MARPLE M D

## THE ANATOMY AND PHYSIOLOGY OF THE BLOOD VESSELS

THE aorta is a wide thick walled tube, the coats of which are rich in elastic tissue When the heart expels blood at high pressure during ventricular systole, the aortic pressure rises The aorta is distended and so accomodates a large portion of the blood expelled from the heart the remainder escaping through the systemic arteries During ventricular diastole the tension exerted by the elastic walls of the aorta maintains the flow of blood onward into the arteries and the aorta diminishes in size until it is distended by the next heart beat Thus the aorta and its larger branches which are similar in structure convert the intermittent output from the heart into the continuous though pulsating flow in the arteries

The arteries into which the blood flows from the aorta divide repeatedly With each subdivision the arterial lumen becomes smaller and the arterial wall becomes relatively more muscular By the contraction or relaxation of these muscular walls the arteries particularly the smaller branches or arterioles, are capable of great variation in caliber It is this variation that determines the proportion of the cardiac output distributed to the various organs

The finest branches of the arterioles are the capillaries, which consist of a single layer of endothelial cells It is through the walls of the capillaries that the interchange of substances between the blood and the tissue spaces takes place

By reason of single muscular elements the capillaries possess the property of independent contractility, mediated by vasoconstrictor nerves and by local chemical or hormonal action The capillaries open and close according to the metabolic needs of the particular tissue in which they lie they react to chemical substances released during the activity of these tissues In resting tissues the capillaries are apt to be almost (or completely) closed during activity they are open Along with the tone of the precapillary arterioles the status of the capillaries determines both the distribution of the blood to the organs and the peripheral resistance

Blood from the capillaries passes through the venules to the systemic veins in which it returns to the heart The veins are large have thinner walls and are less muscular than the arteries They offer little resistance to the flow of blood They are capable of constricting or relaxing in response to vasomotor control They contain valves which prevent a retrograde flow of blood away from the heart Contraction of skele

tal muscles around the veins assists in forcing the blood on its way to the heart When the muscles relax the tension on the veins is relieved and blood flows freely from the arterial side of the circulation toward the heart The action of the skeletal muscles is an important mechanism for facilitating the venous return to the heart and for increasing the output of the heart during exercise

### Factors Determining the Arterial Blood Pressure

The general arterial pressure is determined by the cardiac output and the peripheral resistance The former depends on the venous return to the heart and this in turn on the relationship between the total blood volume and the capacity of the circulatory bed

The peripheral resistance is largely determined by the diameter of the smaller arteries and arterioles and to a lesser extent, the capillaries It is in these vessels that the greatest fall in pressure occurs The state of contraction or tone of the peripheral vessels is controlled by the vasomotor nerves and by the action of certain chemical substances released generally into the circulation or locally from the active tissues Blood viscosity is also a factor in determining peripheral resistance

### The Nervous Control of the Blood Vessels

This is chiefly effected through the autonomic nervous system The sympathetic fibers are adrenergic, the parasympathetic fibers cholinergic and the two have inverse actions on the vessels In the regulation of vascular tone however the sympathetic fibers are by far the more important Stimulation of sympathetic fibers produces vasoconstriction but the degree of constriction varies in different organs The arteries are affected more than the veins or the capillaries It is apparent that there is a steady stream of vasoconstrictor impulses passing along the intact sympathetic fibers since section of these fibers results in an increase of the blood flow through the organ supplied by them Vasodilator impulses transmitted by the sympathetic and parasympathetic systems are of secondary importance

Vasomotor tone is maintained through the mediation of a vasomotor center in the medulla in the floor of the fourth ventricle Stimulation of this area results in generalized vasoconstriction and a rise in blood pressure Section of the brain below this level leads to generalized vasodilatation and a fall in blood pressure The activity of this center in maintaining vasomotor tone is modified by the influence of afferent impulses arising from receptors in the vascular system by impulses from the cerebral hemispheres and by chemical stimuli as for example, by hypercapnia and anoxia

Simple vasodilatation in any organ lowers the peripheral resistance and hence the arterial pressure and increases the capacity of the circulation thus reducing the venous return to the heart and consequently the cardiac output Uncompensated and extensive vasodilatation produces irreversible peripheral circulatory failure or shock Ordinarily this situation is prevented by the compensatory mechanism of the vasomotor reflexes by which vasodilatation in one part of the body is compensated for by vasoconstriction elsewhere Two of these vasomotor reflexes are constantly in action to ensure that the arterial pressure is maintained at a suitable level These are (1) the depressor reflex and (2) the carotid sinus reflex

In the former a rise of pressure in the arch of the aorta stimulates nerve fibers ascending in the vagus trunk from the arch of the aorta to the hind brain Stimulation of these fibers slows up the heart and reduces blood pressure The slowing up of the heart is due to reflex augmentation of vagal tone and to reflex inhibition of sympathetic tone The fall in blood pressure is due to a generalized vasodilatation independent of the cardiac deceleration

If the carotid sinus is stimulated by external pressure or by an increased pressure of the blood within it or by stimulation of the sensory nerve to it there is again a reflex slowing up of the heart and a fall in blood pres ure Conversely, if the pressure of the blood in the sinus is reduced there

is an acceleration of the heart and a rise in blood pressure The reflex arc consists of the glossopharyngeal nerve (afferent), the cardio inhibitory and vasomotor centers, and the vagus and sympathetic nerves (efferent)

Reflex changes also occur in response to temperature changes The loss of heat from the body is regulated by the rate of blood flow through the skin and this, in turn, is controlled by sympathetic nerves A rise or fall in the temperature of the blood stimulates a central mechanism that produces cutaneous vasodilatation or vasoconstriction A secondary factor is the reflex cutaneous vasoconstriction which results from stimulation of cold receptors in the skin In man, the flow of blood through the muscles is not altered by environmental temperature unless shivering occurs

### Chemical Regulation of the Circulation

Epinephrine is released into the circulation from the adrenal medulla during fright asphyxia and muscular exercise and probably through the carotid sinus and depressor reflexes when the blood pressure falls It has a powerful effect on the circulation an effect closely resembling that of a generalized stimulation of the sympathetic nerves

In man small doses increase cardiac output, produce intense constriction of the arterioles capillaries and veins of the skin increase the rate of blood flow through voluntary muscles reduce the blood flow through the kidneys by constricting the efferent arterioles of the glomeruli and elevate the systolic blood pressure while the diastolic pressure remains stationary or falls Larger doses elevate both the systolic and diastolic blood pressures The effect is thus to divert blood from quiescent organs to active organs and to the brain and the heart

The cortex of the kidney contains an enzyme renin which upon intravenous injection produces a prolonged rise of arterial blood pressure This substance will be discussed in a section devoted to the humoral theory of hypertension

Finally it is important to remember that a given stimulus, whether chemical or nervous, produces different effects on the blood vessels supplying different tissues The various organs of the body have quite different roles in the body's economy, and the vessels supplying each organ are adjusted to the appropriate role

## THE NORMAL BLOOD PRESSURE

It is generally accepted that the upper limits of normal blood pressure regardless of age sex or other factors are 140 mm Hg for the systolic pressure and 90 mm Hg for the diastolic pressure Normal blood pressures for the population in general have never been classified according to age or sex The values generally cited are obtained either from insurance statistics or from statistics based on studies of relatively large groups of selected types of persons such as college students hospital out-patients and the inmates of institutions These values though probably representative are subject to selection and error in sampling

## ABNORMALITIES OF BLOOD PRESSURE

The blood pressure is lower during infancy and childhood than during adult life and in childhood does not differ between the sexes Between the ages of 20 and 40 the average systolic pressure is 120 mm Hg in the male and about 113 mm Hg in the female After the age of 40 there is a gradual increase in the systolic blood pressure to an average of approximately 136 mm Hg at the age of 60 Normally there is no concomitant rise in the diastolic pressure during this period nor does the systolic pressure rise above 140 mm Hg Average blood pressures for all ages are roughly 120-125 mm Hg systolic and 80 mm Hg diastolic

Since the blood pressure is a dynamic fluctuating physiological response it is constantly variable within certain limits Not only do environmental conditions modify the blood pressure at any given instant but so do conscious and subconscious nervous influences In the normal

person under controlled conditions both the systolic and the diastolic pressure may vary from 15 to 20 mm Hg over a 24 hour period Fluctuations in pressure are smallest in persons whose blood pressures under basal conditions are low in the normal range, the fluctuations are greater in persons with high normal pressures and are exaggerated in persons with even mild hypertension

When normal subjects are studied by means of the cold pressor test the rise in blood pressure is transient and rarely exceeds 15 mm Hg systolic and 10 mm Hg diastolic In persons with early hypertension and in some persons with normal resting pressures there is an exaggerated response to this test the rise in the blood pressure is two or three times greater than that ordinarily anticipated The rise and fall are so rapid however that the pressure returns to normal within a minute Three quarters of persons so responding have immediate ancestors who have had hypertension There is some evidence not yet conclusive that most of these patients will eventually develop classical hypertension

When hypertension becomes established, the response to the cold pressor test is frequently exaggerated often to as much as from 60 to 100 mm Hg

## HYPERTENSION
### (High Blood Pressure)

Hypertension may be defined as the more or less persistent elevation of the blood pressure above the accepted range for age sex and body weight There are two kinds of hypertension—the primary or idiopathic which is generally known as essential hypertension and the secondary or symptomatic which occurs as a manifestation of one or another of a variety of pathological states The distinction between the two is extremely important for the treatment of primary hypertension is entirely symptomatic whereas successful management of secondary hypertension is not infrequently possible through proper treatment of the predisposing disease From 85 to 95 per cent of all cases of hypertension are of the essential type

*Classification* —A simplified classification of the causes of hypertension appears in the accompanying table 46 I H Page has listed 47 known causes In some instances however the elevated blood pressure may be an associated condition rather than an etiologically related one

TABLE 46 —THE CLASSIFICATION OF HYPERTENSION (After Herndon)

1 Essential
   Benign
   Malignant
2 Nephritic
   Parenchymal
   Vascular
   Perinephritic
   Obstructive
3 Symptomatic
   Physiological
      Pain exertion emotion
   Cerebral
      Increased intracranial pressure
      Diencephalic stimulation
      Lesions in the brain stem
   Cardiovascular
      Aortic regurgitation
      Heart failure
      Arteriosclerosis
      Coarctation of the aorta
      Arteriovenous fistula
      Polycythemia
      Carotid sinus depression
   Endocrine
      Pituitary
         Basophilic adenoma
      Adrenal
         Hyperplasia
         Pheochromocytoma
         Cortical tumors

## ESSENTIAL HYPERTENSION
### (Arterial Hypertension Hyperpiesia)

Essential hypertension or hyperpiesia (Allbutt) has been defined by Ayman as an inherited disease in which the only demonstrable primary change is an elevation of blood pressure due to a functional generalized spasm of the arterioles with the cause of this constriction generally unknown Goldring and Chasis define it as a clinical entity in which an unknown pressor mechanism initiates vasoconstriction elevated blood pressure and vascular sequellæ The fundamental alteration is an increased resistance to the flow of blood in the systemic arteriolar bed consequently the essential

criterion for diagnosis is an abnormal elevation of the diastolic blood pressure. Ordinarily the systolic blood pressure is also elevated and the pulse pressure widened.

Essential hypertension is fundamentally a diagnosis by exclusion, exclusion of conditions commonly accompanied by the appearance of symptomatic hypertension—namely the inflammatory renal diseases, obstructive uropathies and certain cardiovascular, neurological and endocrine diseases. The secondary forms of hypertension are discussed later.

*Incidence.*—The incidence of essential hypertension is high. Among persons of college age, it is reported to occur in between 5 and 20 per cent. In general it occurs in about 7 or 8 per cent of the population. Some 25 per cent of all deaths of persons over 50 are due, directly or indirectly, to hypertension. This is a conservative estimate since renal, cardiac and cerebral deaths are often not attributed to the hypertension which is primarily to blame.

*Etiology.*—The cause of essential hypertension is unknown, but certain factors that contribute to the development of the condition are known.

*Heredity.*—In most cases there is an inherited predisposition to the development of hypertension. This has been noted by various authors and recent studies show that *cardiovascular disease is frequent among* the relatives of hypertensive patients, more particularly among immediate ancestors and siblings.

Hines and Brown studied this hereditary tendency to hypertension by means of the cold pressor test and concluded that the "abnormality of essential hypertension is a hereditary one which appears early in life and remains during life."

It seems evident that individuals whose blood pressures rise to abnormal levels under any circumstances are predisposed in varying degrees to the development of hypertension.

*Age.*—About 90 per cent of all cases of essential hypertension occur after the age of 40 years, from this age onward there is a steady increase in the incidence. Under the age of 30, glomerulonephritis is a far more common cause of elevated blood pressure and essential hypertension is uncommon.

*Sex.*—Despite conflicting statistics it appears that essential hypertension is somewhat more common among women than among men. This greater frequency of hypertension among women may be explained on the basis of previous occurrence of pyelonephritis or toxemia of pregnancy.

The toxemias occur more frequently among persons predisposed to hypertension and, in a high percentage of cases, the hypertension developed or aggravated during pregnancy persists permanently.

*Race.*—Essential hypertension is rare among certain Oriental races and native African Negroes. The children of Negroes who have intermarried with whites, however, are unusually subject to hypertension. Hypertension appears also to be more common among Jews than among Gentiles.

*Infections.*—There is no convincing evidence to show that focal infection contributes to the development of hypertension. Streptococcal infections, including scarlet fever, may lead to acute glomerulonephritis which, in turn, leads to hypertension. This, however, is not essential hypertension.

*Diet.*—Essential hypertension has been related by some observers to excessive protein in the diet. The Eskimos, however, an almost completely carnivorous race, show *no tendency to either hypertension or* cardiovascular renal disease.

*Psychosomatic factors* and *nervous* influences play an important role in the development and course of essential hypertension: (1) the changes that occur in the blood pressures of essential hypertension patients during periods of emotional stress are excessive; (2) during such episodes there is usually other evidence of profound sympathetic nervous stimulation including generalized arteriolar constriction, presumably mediated through the vasomotor center and the sympathetic nerves; (3) that this mechanism bears a causal relation to hypertension is suggested also by the effect of sympathectomy on hypertension, the basal blood pressure and the pressor response to emotional influences being generally reduced after the operation; and (4) success frequently results from the treatment of essen-

tial hypertension with sedatives through emotional and physical rest, and by suggestion

Essential hypertension is manifested first in many patients by exaggerated fluctuations in the blood pressure, fluctuations that can be related in degree as well as in time to the emotional status of the patient The personality and the emotional make-up of the hypertensive patient is of a special type which has existed since childhood, long before the appearance of hypertension Such vague symptoms as headache and nervousness also exist long before the appearance of sustained hypertension

Emotional upsets produce constantly recurring constriction of the arterioles as a result of sympathetic action There is a gradual hypertrophy of the smooth muscle in the arterioles and a gradual but progressive rise in the resting blood pressure The blood pressure finally remains elevated during periods of emotional tranquility and reacts to emotional outbursts in an even more exaggerated manner

The emotional lives of hypertensives correlate often with the onset and early course of their hypertension Faulty adaptation to the difficulties of life lead to emotional disturbances manifested by symptoms whose nature degree and extent depend on the intensity, and duration of the trauma and the susceptibility of the individual Psychoneurotic symptoms are (1) often multiple widespread and do not conform to any clinical entity (2) there are usually associated symptoms and signs of emotional instability such as irritability inability to concentrate excitability and attacks of weeping (3) physical examination is either negative or insufficient to explain the symptoms (4) there is a close relation between periods of stress and appearance of symptoms Clinical observation and the success of psychotherapy confirm diagnosis

The following evidence indicates that hypertensive patients fulfill these criteria (1) Most patients with early hypertension give history of emotional conflict dating back into infancy or early childhood (2) Personality studies show marked emotional responses to ordinary incidents of life (3) New symptoms often follow closely flare ups of old problems or appearance of new problems (4) Many patients exhibit a history of psychosomatic imbalance and of high blood pressure in their families (5) Early symptoms are often relieved by removal of environmental difficulties sedation and suggestion The fundamental mechanism is thus unexplained but may be an endocrine imbalance in which there is an altered pattern of reaction to stress

*Other Factors* — Toxic factors have been suggested as a cause of hypertension but the evidence is not convincing Glandular disturbances have also been suggested as a cause, and these do of course play a primary role in certain types of secondary hypertension But there is no evidence to show that they are important in essential hypertension The use of tobacco has not been shown to have any etiological relationship to hypertension

## Humoral Mechanism of Renal Origin

The experimental work of Goldblatt I H Page and others has emphasized and popularized the fact that persistent hypertension can be induced in various species by constriction of both main renal arteries or constriction of one main renal artery and extirpation of the contralateral kidney This type of experimental hypertension has suggested that elevation of the blood pressure in man may be due to renal vascular disease or any other kind of renal disease that has similar effects on the renal circulation The essential change in renal hemodynamics accompanying hypertension is a reduction in renal blood flow but with a maintenance of glomerular filtration This means that the systemic blood pressure must be increased The interference with renal blood flow must be distal to the glomeruli in the glomerular efferent arteries the changes in the afferent arteries are secondary

Hypertension which follows constriction of the main renal arteries must be humoral in nature and renal in origin Renal denervation and all types of sympathetic nervous interruption fail to prevent or abolish this type of hypertension Transplantation of the kidneys to the other parts

of the body with complete section of all nervous connections does not abolish the hypertensive response. Obstruction to the renal veins at the time of renal arterial constriction does prevent the appearance of hypertension. Finally, blood from a kidney whose main renal artery is constricted is itself vasoconstrictor and pressor.

The renal pressor substance is renin, a proteolytic enzyme elaborated by the kidney. When renin is injected intravenously into the experimental animal, a rise in blood pressure follows promptly, and this effect is not abolished by the removal of any or all of the viscera excepting by bilateral adrenalectomy, following which there is a progressive decline in the pressor response to the injection of the renin.

Renin itself is not pressor, but it reacts in the blood stream with a heat labile, nondialyzable pseudoglobulin preangiotonin (hypertensinogen, renin activator or hypertensin precursor) to form angiotonin (hypertensin). Preangiotonin is apparently formed in the liver. The amount of this substance circulating in the blood is increased in experimental renal hypertension and in human essential hypertension.

Angiotonin is thermostable and dialyzable. Its physiological effects are similar to those produced by the injection of renin intravenously in experimental animals. Angiotonin circulating in the blood stream produces arteriolar constriction sufficient to raise the peripheral resistance. The blood flow is maintained however by the augmentation of the cardiac work.

There is a mechanism that interferes with this phenomenon. Normal serum contains an enzyme, hypertensinase, which is found in large amounts in the renal cortex and in the intestinal mucosa and in moderate amounts in the pancreas, the spleen and the liver. Hypertensinase may suppress the effects of hypertensin. Hypertensinase disappears almost completely from the circulation of dogs who have undergone nephrectomy.

The humoral theory of hypertension may be outlined briefly as follows. Decreased renal blood flow, presumably due to arteriolarsclerosis, reduces the pulse volume in the renal parenchyma. The vascular changes produce renal cellular damage particularly in the tubules and renin is released into the blood stream. Renin interacts with preangiotonin to form angiotonin, which produces a generalized arteriolar constriction sufficient to raise the peripheral resistance. The blood flow is maintained by increased cardiac effort. The effect on the various systemic arteries in the body varies according to the particular qualities of each system. In the kidneys there is further impairment of the hemodynamics and a vicious cycle is compounded since more renin is produced. Hypertensinase may act as a physiological counter measure.

HUMORAL MECHANISM OF RENAL ORIGIN AS A CAUSE FOR HYPERTENSION

| RENIN | + PREANGIOTONIN → | ANGIOTONIN |
|---|---|---|
| (Renal Pressor Substance) | (Renin Activator Hypertensin Precursor) | (Hypertensin) |
| (A proteolytic enzyme of renal origin not directly pressor) | (A plasma globulin of hepatic origin) | (The active pressor agent) |

MECHANISM FOR COMBATTING THE HUMORAL CAUSE FOR HYPERTENSION

| ANGIOTONIN | + HYPERTENSINASE → | Inactive substance |
|---|---|---|
| (Hypertensin) | (Angiotonase) (An enzyme of renal and perhaps other origins) | |

(After John F. Fulton, Textbook of Physiology, p. 906, W. B. Saunders & Co.)

One of the more important controversies about the humoral theory is concerned with the rôle of renal disease and renal ischemia in the production of hypertension. It is well known that not all cases of hypertension are accompanied by arterial and arteriolar sclerosis, nor are all instances of vascular sclerosis accompanied by hypertension. Essential hypertension has been observed repeatedly in man when there has been no evidence of renal ischemia or of preexisting altered renal physiology. This may indicate no more than that renal dysfunction precedes renal pathology. Many observers feel that the primary renal origin of essential hypertension is not proved and that the observed renal ischemia is a sequel to and not a cause of essential hypertension.

Recently Shorr, Zweifach and their associates have reported the regular participation in both experimental renal and human essential hypertension of two hitherto undescribed humoral vasoactive principles which they have termed VEM* and VDM.** VEM is of renal and VDM of hepatic origin, both factors appearing normally

* VEM—Vaso-Excitor material. Chemically called Ferritin.
** VDM—Vaso-Depressor material.

only under anaerobic conditions. Their vascular effects are exerted on the muscular vessels—the metarterioles and precapillary sphincters—of the terminal vascular bed. VEM potentiates the response of these vessels to topically applied epinephrine and enhances their spontaneous constriction and dilatation. VDM exerts exactly opposite effects on the same capillary vessel. On the basis of these vascular actions, the workers suggest that VEM and VDM constitute a homeostatic system contributing to the regulation of peripheral vascular behavior.

In the normal state, neither factor is detectable in blood. According to the findings of these workers in experimental renal hypertension, VEM appears in high concentrations in the blood stream during the acute stage. This results from a renal metabolic defect as a consequence of which VEM formation is no longer confined to the anaerobic state but takes place in oxygen as well. When the blood pressure stabilizes itself at the chronic hypertension level, the humoral VEM is accompanied by physiologically equivalent amounts of VDM continuously released by the aerobic liver. This aerobic formation of VDM by the liver is presumed to be a homeostatic response to sustained high concentrations of VEM in the blood stream.

Schorr, Zweifach and their associates have demonstrated the appearance of both VEM and VDM in the circulation during the hypertensive syndrome and their disappearance when the blood pressure returns to normotensive levels after removal of the renal artery clamps.

They have found that both principles are also regularly present in chronic human essential hypertension in approximately the same amounts as in experimental renal hypertension. The renal origin of VEM and the hepatic origin of VDM in man has been established by bioassays of blood obtained by catheterization of the renal and hepatic veins. VEM and VDM are also present in the blood during the hypertension of Cushing's syndrome and the hypertension of toxemia of pregnancy. In the latter case they disappear on resumption of normotensive levels after delivery.

The exact role of these vasoactive principles in the evolution of the hemodynamics of the hypertensive state still awaits clarification. Unlike hypertensin, which, through its action on the arterioles, exerts acute effects on blood pressure, these principles would be expected to exert chronic effects, effects exerted initially on the capillary muscular vessels and secondarily on the arterioles (which are more directly responsible for increases in peripheral resistance).

## Pathology

The pathological changes of hypertension consist of those changes in the cardiovascular system which occur in response to overwork or strain. Their extent depends upon both the degree of strain and its duration. They are essentially the same in all types of hypertension, although the details may vary in accordance with associated or complicating disease processes. In the early stages of essential hypertension there are no demonstrable structural changes, thus indicating that the primary etiological disturbance is functional.

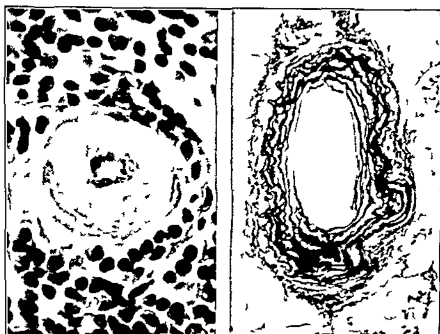
*The Arteries.*—The primary lesion in hypertension is a diffuse hyperplastic arteriolar sclerosis, a hypertrophy of the intima, the internal elastic lamina, and the media. The intima shows hyperplasia and a hyaline thickening of the subendothelial layer. The internal elastic lamina shows a dramatic multiplication and reduplication. The media shows a thickening and hypertrophy of the muscle fibers and a proliferation of the connective tissue. These changes, particularly those in the intima, narrow and at times obliterate the lumen of the vessel. Subsequently degenerative changes, chiefly fibrosis and the deposition of fat, occur. The adventitia is not involved.

These vascular changes are usually diffuse but not generalized. They are almost always more frequent and more pronounced in the kidneys than in other organs. They represent a hyaline degeneration of the vessel wall and are the usual picture of the arterioles in benign hypertension.

As the process advances and the blood pressure rises, there is an accelerated stage in which increased cellular proliferation occurs within the intima.

The new cells are loosely connected by delicate collagen fibrils and are arranged in concentric layers, often piling up so that they encroach upon the lumen, which is partially or completely occluded.

The final or malignant phase of hypertension is characterized by the appearance of necrotizing lesions. The vessel walls lose their outlines as fibrinoid changes occur and focal areas of necrosis appear in the intima. These changes are accompanied by cellular degeneration, diffusion of blood, and the infiltration of polymorphonuclear and mononuclear cells, fibroblasts and pigment laden macrophages. The end result is partial or complete occlusive thrombosis.



FIGS 166–167 —Arterial changes in hypertension (Boyd s Textbook of Pathology )
FIG 166 —Hyaline degeneration × 510 FIG 167 —Elastic hyperplasia × 500

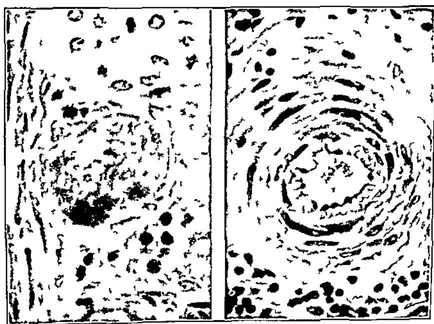


FIG 168 —Arteriolar necrosis × 430 FIG 169 —Cellular hyperplasia × 340

Hypertension is essential to the development of such lesions but not to the development of atherosclerotic changes in the aorta and other great vessels or for the calcareous changes in many of the medium sized arteries Such changes characteristic of arteriosclerosis frequently accompany hypertension, but they do not always do so and are not an integral part of the pathology of hypertension

emia secondary to an inadequate blood supply to the hypertrophied myocardium

*The Kidneys* — The essential lesion in the kidney is a thickening and narrowing of both the efferent and the afferent arterioles and the characteristic subintimal deposition of hyaline in these vessels This is the earliest lesion found in patients with hypertension These vascular changes lead to an obliteration and fibrosis of the glomeruli and

TABLE 47 —THE GROUPING OR GRADING OF ESSENTIAL HYPERTENSION
(After Wagener and Keith)

| | *Group I* *Early or Mild Benign* | *Group II* *Moderate Benign* | *Group III* *Late or Severe Benign* | *Group IV* *Malignant Syndrome* |
|---|---|---|---|---|
| *Age* | 30 to 6[illegible] | 21 to 59 | 2[illegible] to 5[illegible] | 8 to 64 |
| Symptoms | None to slight Health good | Slight Early morning headaches vertigo General health good | Definite Headache nervousness vertigo tiredness dyspnea nocturia | Severe Headaches disturbed vision muscle pains weakness dyspnea |
| Blood pressure | Systolic 150 to 200 Diastolic 100 to 1[illegible]0 Occasionally normal at rest | Systolic 200 to 2[illegible]0 Diastolic 100 to 130 Lower at rest but never normal | High Almost always over 1[illegible]0 systolic and 110 diastolic | High and fixed Systolic usually over [illegible]50 diastolic seldom below 140 |
| Retinal Changes | None or minimal arterial narrowing | Definite arteriolar sclerosis Arteriovenous compression No retinitis | As before plus retinitis with edema white spots cotton wool patches and hemorrhages | As in group 3 plus papilledema |
| Heart | Slight or no demonstrable change | Slight enlargement Left ventricular preponderance Good function | Enlarged Definitely diminished reserve | Enlarged Actual or impending failure |
| Urine | Normal | Mild albuminuria and casts | Albumin casts and often red cells | Albumin casts and red cells |
| Renal Function | Normal | Slightly decreased Urea clearance 30 to 40 cc | Decreased Urea clearance 20 to 30 cc | Function usually low with urea clearance [illegible] to [illegible]0 cc |
| Brain | Normal | Normal | Cerebral disturbances or accidents frequent | Disturbances present |
| Five Year Mortality | 30 per cent | 4[illegible] per cent | 80 per cent | 99 per cent |

*The Heart* —Initially the heart shows concentric hypertrophy with left ventricular preponderance due to enlargement of the individual muscle fibers in the wall of the left ventricle Persistent cardiac strain results eventually in dilatation As the left side of the heart fails, increased pressure in the pulmonary circulation increases the load on the right ventricle, which then undergoes similar changes

Hypertrophied hearts show some evidence of muscle damage fibrosis atrophy and the deposition of lipoid material but these changes are attributed to an associated nutritional deficiency most probably anox-

subsequently to atrophy of the involved tubules The end result is a true granular primary contracted kidney since the condition is primarily vascular and not renal

There is eventually a tremendous increase of connective tissue in the kidneys replacing the destroyed parenchyma and arising in part from nutritional changes due to the impaired circulation The process is characteristically patchy so that areas of essentially normal or hypertrophied renal tissue may be seen amidst areas of advanced atrophy and fibrosis It is this alternation which accounts for the grossly granular surface and irregular cortex

The urine from these kidneys contain a little protein and a few casts. When many of the glomeruli have been destroyed, the kidneys lose their ability to concentrate urine. Renal function tests show that in the terminal stages all renal functions are depressed and there is an increase in proteinuria.

Malignant hypertension tends to terminate in uremia. In these cases, there is a marked hyaline and collagenous thickening of the intima of the arterioles, areas of intimal necrosis, and thrombotic occlusion of many afferent glomerular arteries, a picture of necrotizing renal arteriolitis. The urine of these patients contains large quantities of albumin and large numbers of casts and erythrocytes. Hematuria is a prominent feature and is often sufficient to suggest actual hemorrhage. It is to be emphasized however that the kidneys of those patients who do not die of uremia do not show more than the usual changes of hypertension.

## Clinical

The general or systemic manifestations of hypertension are those of chronic fatigue—both nervous and physical. Mentally, there is irritability, depression, fatigability, loss of concentration, worry and insomnia. Headache is a common complaint at all stages of the disease and under a variety of circumstances. It is probably of diverse origins as is discussed in the section on cerebral symptoms. That many symptoms arise on a vasomotor basis is evident in many instances where there are visible stigmata of vasomotor instability. Local symptoms arise most frequently from cerebral, cardiac or renal involvement.

*Cardiac.*—The clinical evolution of the heart in hypertension is characteristic. Hypertension, especially if benign, may exist for a long period of time without the development of cardiac enlargement. Then the heart begins to enlarge at first to the left, later toward the right as well. To a certain point no murmurs appear but the apical beat becomes forceful and the aortic second sound is accentuated and ringing. During the progressive enlargement of the heart, as the valve rings stretch and the heart chambers dilate, murmurs appear. Characteristically a systolic murmur appears at the apex, later an aortic systolic or diastolic murmur may occur along the left sternal border. Disturbances in rhythm are apt to appear, usually extrasystoles, auricular fibrillation or, less commonly, flutter. Since the essential strain is on the left ventricle, the chief symptom is ordinarily dyspnea, followed by the classical stages of left heart failure, paroxysmal dyspnea, cardiac asthma and pulmonary edema. Right heart failure occurs eventually and with it the appearance of generalized edema. There is often a complaint of a dull precordial ache. True angina pectoris is ordinarily due to the complicating coronary sclerosis which occurs clinically in at least half the patients with hypertension.

## Cerebral Symptoms

The cerebral symptoms which accompany hypertension may be discussed conveniently in four general groups.

1) *Functional Symptoms.*—These symptoms include throbbing sensations, vertigo, headaches, mental fatigue, failure of concentration, irritability and the like which may occur before there is evidence elsewhere of vasospastic or organic vascular changes. There may be impairment of memory. Headaches are commonly occipital in location and usually appear in the mornings. Preexisting migraine is aggravated. Many of these symptoms are common to any condition of ill health.

2) *Vascular Symptoms.*—These symptoms are due to structural alterations in the cerebral vessels and to hemorrhage or thrombosis. They occur largely in older patients in whom arteriosclerotic changes have usually occurred in the vessels. Cerebrovascular accidents (*e.g.* spasm, hemorrhage or thrombosis) may produce syndromes ranging from slight transient episodes of numbness and tingling in the extremities, mental confusion and aphasia to hemiplegia and death. Milder attacks tend to clear without residual effects; even a patient with hemiplegia may recover completely. Following severe attacks, mental changes

(impaired memory, loss of concentration irritability, *etc*) usually persist

The role of cerebral vascular spasm in these cases is not entirely clear. It may be deduced from the fact that there is retinal arterial spasm in many instances. It is suggested also by the transitory and varying nature of the focal cerebral symptoms. It is probably but one manifestation of a generalized vasoconstriction which manifests itself at such times by an increased blood pressure. Pathologically there is support for this theory in the appearance of the brain which is pale, relatively bloodless and edematous.

3) *Uremic Symptoms*.—These symptoms appear in those cases in which progressive renal failure is the dominant complication. There is a progressive general depression and apathy which leads from drowsiness into stupor. The patient can be aroused only with difficulty and is disoriented and delirious. Finally coma supervenes with deep (Kussmaul) breathing and terminally stertorous breathing which may be punctuated by periods of apnea. Tremors, twitchings and clonic convulsions are common terminally.

4) *Hypertensive Encephalopathy*.—These cerebral changes occur most frequently when there has been a rapid rise in the blood pressure above its previous high levels. They are usually associated with papilledema. The clinical manifestations are those of focal or diffuse cerebral disturbances. Commonly there are severe headache, nausea and vomiting, convulsions and apathy, somnolence or coma. Less frequently paresthesias, amaurosis, aphasia and hemiplegia occur. These symptoms and signs may occur individually or in any combination. The attacks are often sudden and dramatic and epileptiform in character like those seen in eclampsia. Other attacks may be protracted for weeks or months so that the clinical picture resembles that of brain tumor. The focal phenomena such as amaurosis, aphasia and paralyses are characteristically transitory. Neurological findings usually include exaggerated tendon reflexes, often positive Babinski signs, and occasional signs of meningeal irritation (stiffness of the neck and legs).

## OPHTHALMOSCOPIC FINDINGS

Ophthalmoscopy is an invaluable aid in the diagnosis and study of cardiovascular and renal disease. In no vascular condition is this more true than in hypertension, since the arterioles throughout the body are the chief point of attack and these can be visualized readily and directly only in the retina.

The vascular changes in the retina in hypertension may be described in several stages.

1) *Pre-organic Stage*.—The earliest change observed in the retinal vessels is that of increased arterial tone in which the lumen

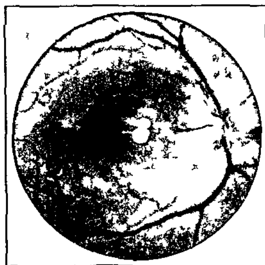


FIG 170.—Arteriospastic hypertensive narrowing of retinal arterioles. (Courtesy of Department of Ophthalmology, Temple University School of Medicine.)

of the arterioles is uniformly narrowed. The constrictions may be localized and are either transitory or variable.

2) *Earliest Organic Changes*.—The first recognizable change in the arterioles is a hypertrophy of the tunica media. This produces a narrowing of the lumen and gives it an irregular appearance. The reflection of light from the wall of the arteriole is increased and produces a coppery or steely appearance. Where the arterioles and veins are in contact, the increased thickness of the arteriolar wall and the increased arteriolar

pressure produce indentations in the readily compressible veins (arteriovenous nicking)

3) *Retinal Arteriosclerosis* —The arterioles are small and narrow and irregularly indented There is an exaggerated light reflex The vascular wall is brightly visible The veins are full and tortuous and are compressed where they are crossed by an artery This compression is at first a nick in the vein, but, later the vein is not visible for a short distance on either side of the point of crossing Finally, when the constriction is almost complete an S shaped twist appears in the vein Where the vein crosses an artery, this curve is distinctly U shaped At this stage there are frequently punctate hemorrhages and white punctate spots of hyaline or fatty degeneration arranged in a radiating manner about the macula The discs are normal or slightly congested, but there is no papilledema

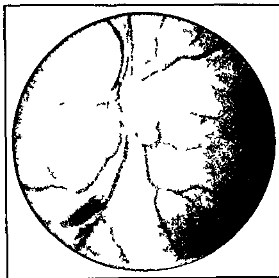


Fig 171 —Mixed sclerotic and spastic hypertensive focal constrictions with retinopathy of hypertension (Courtesy of Department of Ophthalmology Temple University School of Medicine)



Fig 172 —Retinopathy of malignant hypertension (Courtesy of Department of Ophthalmology Temple University School of Medicine)

4) *Hypertensive Neuroretinitis* (*Vasospastic or Albuminuric Retinitis*) The characteristic findings in hypertensive retinitis are cotton wool patches edema of the nerve fibers distal to the points of arteriolar narrowing occlusion, or spasm The arterioles are small and almost bloodless There is dilatation and stasis of the capillary bed resulting in serous and hemorrhagic transudations into the retina Flame shaped hemorrhages are usually present This stage of retinitis may be superimposed upon any preceding stage of organic change and a similar picture occurs in the terminal stages of glomerulonephritis It may also follow a pure vasospastic retinitis in which there is an absence of organic changes in the arterioles as in toxemia of pregnancy or in acute arterial hypertension and in these the changes may regress to the point of normality

5) *Papilledema* —The final stage is the development of papilledema which indicates the presence of increased intracranial pressure resulting from cerebral edema The discs may attain a height of 4 diopters or more

## Laboratory Findings

1) *X ray of the Heart* —The existence of minimal degrees of cardiac hypertrophy in the early stages of hypertension cannot always be determined roentgenologically but a preliminary film is of value in ascertaining whether or not the cardiac shadow is widened for purposes of comparison with later films Periodic roentgen examinations will then disclose the rate of cardiac enlargement

2) *X rays of the Kidneys* —Roentgen examination of the kidneys, utilizing intra

venous urography, may reveal abnormalities of the urinary tract in patients with hypertension, but it is seldom that the abnormalities prove to have any relation to the hypertension If the examination of the urine and renal function studies are normal roentgen examination of the kidneys should be done only on the basis of some other indication If these studies are abnormal indicating a possible renal origin for the hypertension urography is advisable

3) *Electrocardiogram* —The electrocardiogram may give the first evidence of an organic change in the heart in response to hypertension Changes characteristic of left ventricular strain appear commonly in the electrocardiogram before there is any apparent enlargement of the heart by roentgen examination

The earliest electrocardiographic picture is that of left axis deviation The characteristic electrocardiographic pattern of hypertrophy is that of so-called left ventricular strain in which there is increased voltage in the R waves depression of the RS-T segment of 0 5 mm or more in lead I and flattening inversion or other definite abnormality of the T wave in lead I Such changes occur in the left arm lead in horizontally placed hearts and in the left leg lead in vertical hearts Slurring of the Q R-S complex occurs subsequently and this may in turn lead to various types of conduction defects

The failure of the coronary circulation to compensate for the increased mass of myocardium to be supplied with oxygenated blood in cardiac hypertrophy and the frequent association of coronary artery disease in the presence of hypertension results in myocardial damage and those electrocardiographic changes characteristic of coronary artery disease

One important use of the electrocardiogram as with the roentgen examination of the heart is to assess the speed and degree to which the heart suffers damage Serial electrocardiograms over long periods of time are of great value in determining the course of the disease as it is reflected on the functional capacity of the myocardium

4) *Renal Function Tests* —The most practical and useful test for renal function is the concentration test by which the power of the renal tissue to concentrate urine is determined The principle of this test is to restrict the fluid intake, but not the ingestion of food for a period of time which permits the kidneys to concentrate the urine to its maximum capacity Special modifications of the test have been described by Volhardt Mosenthal Fishberg and Ayman

Formed elements may not appear in the urine of patients with hypertension until there has been renal impairment of a considerable degree and for a prolonged period of time except in malignant hypertension when urinary abnormalities may appear promptly and dramatically The concentration test may be supplemented when indicated by other tests of renal function the blood urea or N P N the phenosulfophthalein test urea clearance diodrast excretion inulin clearance creatinine clearance *etc*

5) *Blood Counts* —Whether anemia or polycythemia exists should be determined by means of a complete blood count in each patient with hypertension

6) *Basal Metabolic Rate* —The basal metabolic rate should be determined in all patients with hypertension who are suspected of having hypo- or hyperthyroidism

7) *Blood Chemistry* —The blood urea or the N P N should be determined in all instances where renal function is suspected of being impaired A fasting blood sugar or a glucose tolerance test should be performed on all patients suspected of having diabetes mellitus The blood-cholesterol level should be studied in patients with significant arteriosclerosis or in those in whom an abnormality of fat metabolism might be present

The circulation time of the blood is normal in cases of hypertension until congestive heart failure supervenes The blood volume and the acid base balance are normal in uncomplicated hypertension The blood proteins are not reduced by hypertension *per se*

## Differential Diagnosis

Hypertension may be produced by or accompany a variety of pathological conditions Essential hypertension affects by

far the greatest number of persons For purposes of discussion, hypertension may be divided into three general groups

1) *Essential Hypertension* — This diagnosis may be made when the patient has abnormally high systolic and diastolic blood pressures in the absence of any renal or other disease which is known to result in an elevated blood pressure It is essentially a diagnosis by exclusion

2) *Renal Hypertension* —(a) *Glomerulonephritis* —The blood pressure is ordinarily elevated during the acute stage of glomerulonephritis and this elevation is, in general in proportion to the degree of activity of the inflammatory process This elevation of blood pressure is essentially a symptomatic hypertension Following the acute stage of glomerulonephritis the blood pressure frequently falls to normal even though the persistence of urinary findings indicates that the renal lesion is still active

During the chronic stage of glomerulonephritis the blood pressure is most commonly normal despite the progression of the renal lesion With the development of the late stage of glomerulonephritis, the blood pressure becomes elevated in about 75 per cent of the cases Its presence indicates that the nephritic process has been complicated by diffuse arteriolar disease within the kidney and this arteriolar process becomes the dominant feature in the progression of the case

Patients with late glomerulonephritis are often indistinguishable from patients with late essential hypertension except that they may give a history of antecedent acute or chronic nephritis The pathological pictures are indistinguishable so that it is impossible to tell on this basis whether the inflammatory or vascular lesions were primary In general patients with glomerulonephritis exhibit greater proteinuria earlier and more pronounced renal failure lower blood pressure and less advanced degrees of cardiac involvement than do patients with essential hypertension who develop renal damage

b) *Toxemia of Pregnancy* —In toxemia of pregnancy (preeclampsia unless convulsions or coma occur) the most constant and characteristic lesion is a diffuse degenerative renal lesion The disease is an acute vascular syndrome, occurring during the latter half of pregnancy and closely resembling glomerulonephritis in producing hypertension, albuminuria, and edema Toxemia of pregnancy occurs in from 5 to 10 per cent of pregnant women whose blood pressures have been normal previously It occurs in over 50 per cent of women whose blood pressures have been elevated previously Permanent hypertension persists in about 25 per cent of the cases and differs in no essential clinically or pathologically from other types of chronic hypertensive disease

c) *Pyelonephritis* —Chronic pyelonephritis with contracted and scarred kidneys is commonly accompanied by hypertension and ultimately renal failure In the late stages these patients cannot be distinguished from those with essential hypertension except on the basis of an adequate history The primary lesion is of course renal and the hypertension is secondary Among the surgical conditions associated with hypertension unilateral atrophic pyelonephritis has been followed by the greatest percentage of permanent reductions in blood pressure when nephrectomy has been performed

d) *Disseminated Arteritides* — Hypertension is present in the disseminated arterial diseases such as lupus erythematosis periarteritis nodosa *etc* only when there is extensive involvement of the renal arteries This suggests of course that the hypertension in these cases is of renal vascular origin

e) *Congenital Polycystic Kidneys* —This congenital lesion is an uncommon cause for hypertension but must be considered in all instances where there is evidence of renal disease Suspicion aroused by the urinary findings and often by the discovery of a palpable mass in the abdomen can be confirmed readily by pyelography

f) *Surgical Renal Disease* —In the instances of hypertension accompanying hydronephrosis urinary lithiasis renal tuberculosis chronic perinephritis and renal tumors (especially Wilm s tumor) the hypertension appears to be related to the extent of the parenchymal damage and to the degree of renal vascular sclerosis rather than to the primary disease Increased back pressure does not produce hypertension unless it is

bilateral and acute. In the presence of a surgical renal lesion it is important to determine whether the hypertension is secondary to the renal pathology, or whether it is an *unrelated coexisting essential hypertension.*

*g) Renal Atherosclerosis.*—The progressive narrowing of the renal arteries by atherosclerosis is frequently associated with hypertension. The experimental studies of Goldblatt and others suggests that there may be an etiological relationship between this *renal arterial narrowing and hypertension.* It is however usually impossible to determine whether the hypertension preceded the atherosclerotic process, or vice versa.

*h) Aneurysm of the Renal Artery.*—We have seen a case of marked hypertension which was relieved completely by removal *of a left kidney and aneurysmal renal artery.* Pathological study of the kidney failed to reveal any changes whatsoever.

3) *Symptomatic Hypertension.*—(*a*) *Physiological Hypertension.* The normal response of the organism to the stimuli of pain, excitement, emotion and exertion is a generalized *vasoconstriction and an increase in the* heart rate producing a transient elevation of the blood pressure. The exaggerated response of many young individuals has suggested that an excessive and oft repeated response of this nature may be a precursor for a sustained and permanent essential hypertension.

*b) Cerebral Hypertension.*—Increased intracranial pressure is commonly accompanied by an increase in the systemic blood pressure. The hypertension which accompanies organic lesions of the diencephalon and the brain stem is probably due to direct stimulation of the vasomotor centers.

*c) Cardiovascular Hypertension.*—Hypertension of a compensatory character may accompany instances of *aortic regurgitation and of polycythemia.* The hypertension which exists in the upper extremities in *coarctation of the aorta* is a physiological attempt to compensate for the diminished blood flow below the obstruction and particularly to the diminished renal blood flow. The hypertension in *arteriovenous fistula* is also *a compensatory mechanism* in response to the shunting of blood from the arterial to venous circulations. In arteriovenous fistula there is an increase in both the cardiac output and the circulating blood volume. The work of the heart is increased so that hypertrophy ordinarily *follows eventually.* Hypertension arising in instances of *advanced arteriosclerosis* is apparently a mechanism which attempts to compensate for the loss of elasticity of the walls of the major vessels. In these cases the systolic blood pressure is elevated and the diastolic blood pressure remains normal *or relatively so. Since the work of the heart* is not significantly increased, cardiac hypertrophy is not a prominent feature.

*d) Endocrine Hypertension. Basophilic adenomas of the pituitary gland* are almost always accompanied by hypertension. *Pheochromocytomas* (paragangliomas) arising *from the adrenal medulla or from the* chromaffin bodies in the paravertebral region may produce *either paroxysmal or sustained* hypertension due to the secretion of excessive amounts of adrenalin into the circulation. Two tests are of considerable value in establishing the presence of such a *tumor: the histamine test and the benzodioxane test.* (For discussion of these tests see Chapter 16.)

*Adrenal cortical tumors* (adenomas, carcinomas) produce hypertension in association with other manifestations of an excessive secretion of adrenocortical hormones. *There is no excessive secretion of adrenalin.* Such tumors produce precocious puberty in children and Cushing's syndrome in adults. In *hyperthyroidism* there is systolic but not diastolic hypertension. The elevated blood pressure is a result of an increase in the force and rate of the heart beat. The blood pressure is not related to the degree of hyperthyroidism and it is not necessarily relieved by thyroidectomy. Hypertension appearing at the time of the *menopause* may be influenced by the suppression of the ovarian secretions but it is not primarily endocrine in origin.

## TREATMENT

The treatment of essential hypertension may *be discussed most conveniently in three* phases—the treatment of symptoms, efforts to reduce the elevated blood pressure, and

far the greatest number of persons. For purposes of discussion, hypertension may be divided into three general groups.

1) *Essential Hypertension.*—This diagnosis may be made when the patient has abnormally high systolic and diastolic blood pressures in the absence of any renal or other disease which is known to result in an elevated blood pressure. It is essentially a diagnosis by exclusion.

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Patients with late glomerulonephritis are often indistinguishable from patients with late essential hypertension except that they may give a history of antecedent acute or chronic nephritis. The pathological pictures are indistinguishable so that it is impossible to tell, on this basis, whether the inflammatory or vascular lesions were primary. In general, patients with glomerulonephritis exhibit greater proteinuria, earlier and more pronounced renal failure, lower blood pressure and less advanced degrees of cardiac involvement than do patients with essential hypertension who develop renal damage.

b) *Toxemia of Pregnancy.*—In toxemia of pregnancy (preeclampsia, unless convulsions or coma occur) the most constant and characteristic lesion is a diffuse degenerative renal lesion. The disease is an acute vascular syndrome, occurring during the latter half of pregnancy and closely resembling glomerulonephritis in producing hypertension, albuminuria and edema. Toxemia of pregnancy occurs in from 5 to 10 per cent of pregnant women whose blood pressures have been normal previously. It occurs in over 50 per cent of women whose blood pressures have been elevated previously. Permanent hypertension persists in about 25 per cent of the cases and differs in no essential clinical or pathologically from other types of chronic hypertensive disease.

c) *Pyelonephritis.*—Chronic pyelonephritis with contracted and scarred kidneys is commonly accompanied by hypertension and ultimately renal failure. In the late stages these patients cannot be distinguished from those with essential hypertension except on the basis of an adequate history. The primary lesion is of course renal and the hypertension is secondary. Among the surgical conditions associated with hypertension unilateral atrophic pyelonephritis has been followed by the greatest percentage of permanent reductions in blood pressure when nephrectomy has been performed.

d) *Disseminated Arteritides.*—Hypertension is present in the disseminated arterial diseases, such as lupus erythematosis, periarteritis nodosa, *etc.*, only when there is extensive involvement of the renal arteries. This suggests, of course, that the hypertension in these cases is of renal vascular origin.

e) *Congenital Polycystic Kidneys.*—This congenital lesion is an uncommon cause for hypertension but must be considered in all instances where there is evidence of renal disease. Suspicion aroused by the urinary findings and often by the discovery of a palpable mass in the abdomen can be confirmed readily by pyelography.

f) *Surgical Renal Disease.*—In the instances of hypertension accompanying hydronephrosis, urinary lithiasis, renal tuberculosis, chronic perinephritis, and renal tumors (especially Wilm's tumor), the hypertension appears to be related to the extent of the parenchymal damage and to the degree of renal vascular sclerosis rather than to the primary disease. Increased back pressure does not produce hypertension unless it i

*Reduction of Blood Pressure* —The desirability of reducing the blood pressure in essential hypertension is open to debate

Undoubtedly it is advisable when symptoms are relieved or ameliorated by its reduction In instances of asymptomatic essential hypertension it has yet to be conclusively proved how much is to be gained by reduction in blood pressure *per se* However it seems logical to lessen the strain on the entire vascular tree

There are three measures for which a brief may be held at present—the medical treatment using thiocyanate, the low sodium low protein diet and the surgical operation of sympathectomy

The potassium ammonium or sodium salts of thiocyanate may be administered to hypertensive patients who exhibit reasonably good renal function and who are not in heart failure These compounds should be used only when facilities exist for the periodic determination of the blood thiocyanate level

One cannot specify a given dosage for any one patient The maintenance doses must be regulated according to the blood thiocyanate level Generally an initial dose of 0 2 gm of potassium thiocyanate given three times a day in the form of enteric coated tablets or capsules for 3 days is followed by 0 2 gm twice a day for 4 days The blood thiocyanate level and the N P N are then determined If the blood thiocyanate level is 6 mg or less the dosage is continued at 0 2 gm twice a day for another week When the blood thiocyanate level exceeds 8 mg the dosage should be decreased to 0 2 gm and 0 4 gm as a total dose on alternate days if the blood level is between 8 and 10 mg or to 0 2 gm daily if the blood level is above 10 mg Within a few weeks it is possible to stabilize the majority of patients at a level of between 8 and 10 mg which is desirable

Determinations of the blood thiocyanate level may then be done at intervals of from 2 to 4 weeks If higher levels between 10 and 12 mg are desired determinations of the blood level should be done more frequently The individual response to thiocyanate varies widely among patients and in the same patient from time to time Extreme caution in the administration of the drug is advised

Toxic symptoms of thiocyanate therapy include fatigability drowsiness and in severe instances coma There may be anorexia nausea and even vomiting Weakness may appear and lead to faintness or collapse Psychoses and skin eruptions have been reported

Thiocyanate therapy will often relieve severe headache if proper blood levels are maintained It will often lower the blood pressure moderately though irregularly and in mild hypertension it may produce a normal blood pressure The effects of thiocyanate wear off 2 or 3 weeks after it has been withheld and the blood pressure then returns to its previous level

Veratrum viride has been used recently for its hypotensive effect but reports of its effectiveness are rather conflicting Dosage is determined empirically by administering gradually increasing doses until therapeutic or toxic effects are observed The preparation is given by mouth and the duration of effect is between 10 and 14 hours One may administer 10 Craw units (1 tablet) every 2 hours until an effect is observed and then maintain the patient on a therapeutically effective maintenance dose every 12 hours A hypotensive effect is achieved in perhaps 50 per cent of patients Symptomatic relief is apt to be greater than objective evidence of improvement Some excellent results have been reported in hypertensive encephalopathy

Toxic effects include nausea and vomiting a sense of constriction in the throat and chest excessive salivation occasional facial and peripheral paresthesias and transient blurring of vision These are encountered in perhaps one third of all patients so treated but the effects usually recede promptly upon the withholding of medication Cumulative toxic effects occur usually with daily doses of 60 or more Craw units and hypotensive effects are closely related to the toxic manifestations The intravenous injection of protoveratrine obtained from Veratrum viride is being studied at the present time

*Low Sodium Diet* —Careful observation of the effects of the low sodium diets during

treatment of impaired function of the various organs damaged by the disease

*Symptomatic Treatment* —Many symptoms of essential hypertension are psychosomatic in nature or are markedly aggravated by the reaction of the patient to the traumatic impacts of life They should be treated in exactly the same manner and with just as much attention to detail as they would be in psychoneurosis on any basis and of any origin Psychotherapy, ranging from detailed psychoanalysis to the necessarily superficial but careful inquiry into the emotional problems of the patient by the attending physician, may produce remarkable improvement in the symptoms presented Sedatives used judiciously are important adjuncts in the treatment of fatigability tension insomnia and related symptoms The barbiturates are used most frequently but sodium bromide or chloral hydrate are excellent substitutes when given in moderate doses at bedtime or in smaller doses on two or three occasions during the day

The vasospastic symptoms, such as headache, vertigo and episodes of peripheral vasospasm, may be relieved by the use of sedatives and the headache itself may respond to the use of analgesics Acetyl salicylic acid preferably in compound pills is the most commonly used agent for this purpose Experience with the sympathetic blocking agents is limited but these may be worth a trial since one of their effects is to produce hypotension

Priscoline® appears to be the most effective of these agents and is effective by mouth, which is an advantage in long term therapy Potassium thiocyanate, which is used to reduce the blood pressure itself is particularly useful in relieving the more severe and persistent headaches and attacks of dizziness This has also been claimed recently for veratrum viride and related compounds In instances where headaches and cerebral symptoms occur so violently as to constitute a crisis intramuscular injections of 50 per cent magnesium sulphate or lumbar puncture with removal of moderate amounts of spinal fluid may afford relief

Impaired cardiac function is a common cause of dyspnea Dyspnea is usually the first symptom of cardiac origin, but dyspnea may occur from other causes and must be evaluated carefully Progressive exertional dyspnea accompanied by cardiac enlargement and electrocardiograph evidence of myocardial damage is almost always due to cardiac damage resulting from hypertension Occasionally, paroxysmal nocturnal dyspnea cardiac asthma, or pulmonary edema may reveal evidence of cardiac failure early in the course of the disease

Patients suffering cardiac failure or severe myocardial damage must reduce their weight to normal if it is excessive Digitalization is indicated in overt heart failure or auricular fibrillation, mercurial diuretics and low sodium diets are necessary when there is evidence of either right- or left sided heart failure Severe dyspnea without overt heart failure often responds to a period of bed rest and a regimen of the purported coronary vasodilators—the xanthines, of which aminophyllin is the most popular

In patients with severe dyspnea and orthopnea but no gross evidence of congestive heart failure the use of the mercurial diuretics is finding increasing favor The action of these agents is often augmented by preparing the patient with ammonium chloride for several days prior to the injection of the mercurial

Nocturia associated with the inability of the kidneys to concentrate the urine indicates impaired renal function Treatment consists in maintaining an adequate intake of fluid and of protein but restricting the intake of sodium In this manner adequate fluid intake may be maintained without increasing edema formation When renal failure is severe one must be cautious lest the restriction of sodium leads to symptoms of acute sodium depletion Mercurial diuretics should not be used in advanced renal failure Anemia may occur in instances of essential hypertension complicated by renal failure and may fail to respond to any measure other than repeated blood transfusions In terminal renal insufficiency treatment is palliative Fluids and salts are replaced by small subcutaneous infusions transfusions are given for anemia calcium chloride for the tetany which may be associated with uremia and bicarbonate of soda for acidosis

*Postoperative complications of sympathectomy* include pneumothorax arising from incision of the pleura at surgery, neuritis, due to injury to the intercostal nerves, and sterility due to inability of the patient to empty the seminal vesicles. Postural hypotension on assuming the erect position is a common occurrence postoperatively in successful sympathectomy. It is accompanied by a disturbing tachycardia and may produce syncope. Ordinarily this effect becomes much less pronounced as time elapses and may disappear completely in from three to twelve months. In some instances this may persist indefinitely and prove sufficiently annoying to require the wearing of an abdominal support.

Though the mortality rate from these procedures is under 10 per cent in the best hands, one of the more common causes of death is coronary occlusion with myocardial infarction. This is thought to be a result of the sudden lowering of the blood pressure.

Sympathectomy can accomplish the following favorable effects. Blood pressure, both systolic and diastolic, may be reduced significantly, and sometimes this is permanent. The size of the heart may be reduced, and the electrocardiogram may revert from the pattern of left ventricular hypertrophy and strain to a normal tracing. Changes in the ocular fundi may regress with relief of arteriolar spasm and clearing of edema of the optic discs. It is not clear how great an improvement may occur in renal function, but the abnormal findings in the urinary sediment may disappear completely following sympathectomy. Even when there is no objective improvement there is frequently a dramatic and sustained improvement symptomatically, including the partial or complete relief of intractable headache. In many patients the improvement is of a temporary nature only.

*The selection of patients for sympathectomy* is uncertain. The edation test, various pressor tests (*e g* cold pressor test), caudal or spinal anesthesia, and the administration of sympathetic blocking agents preoperatively to patients with essential hypertension have not proved to be of any consistent value in selecting patients for sympathectomy. Careful observers have concluded that the number of patients who are suitable candidates are fewer than 10 per cent of all patients with hypertension.

Sympathectomy should not be performed for the relief of symptoms unless these are unendurable and cannot be relieved by other less heroic measures. It should be performed only by highly skilled specialists experienced in this procedure. Sympathectomy is rarely or never an emergency and so should always be preceded by painstaking evaluation of the patient and his disease.

There is no convincing evidence that the life expectancy of hypertensive patients is improved by this procedure.*

### Prognosis

Essential hypertension is ordinarily a progressive disease and the prognosis in any given case must, of necessity, be guarded. One may quote statistics at length but they are of small avail in the individual case.

The prognosis in general appears to depend on several major and several minor factors.

1) *Major Factors.*—(*a*) The extent of the arteriolar lesions can be determined most accurately by examining the retina and by determining the functional state of the kidneys.

*b*) The degree of arteriosclerosis present. Degenerative changes always occur in the larger arteries and they are more closely related to the duration of the hypertension than to its degree. Such lesions, involving especially the coronary and cerebral arteries, are frequently the factors determining the course and outcome of the disease.

*c*) The integrity of the heart, which depends on the efficiency and sufficiency of the coronary circulation.

2) *Minor Factors.*—(*a*) The height of the blood pressure.

*b*) The age at which hypertension develops. Hypertension developing in middle and old age is usually milder and more slowly progressive than is hypertension developing in early life, since in early life it tends to run a more rapid course and often terminates in the syndrome of malignant hypertension.

*Partial adrenalectomy in combination with sympathectomy has been found a useful procedure in reducing severe malignant hypertension that is otherwise intractable, but whether this procedure produces a lasting beneficial effect is not yet known. For discussion of adrenalectomy in hypertention *see* C. C. Wolferth *et al.* Ann Int Med 35 July 1951.—Editor

the past 15 years seems to warrant the following statements

1 Some patients with severe essential hypertension will respond to a very low sodium diet with a significant reduction in blood pressure and may maintain the reduction while they remain on the diet, in some cases as long as several years

2 Associated with this reduction in blood pressure the eye signs and the untoward symptoms of hypertension may disappear or markedly improve

3 It is impossible at present to predict with certainty before trial which patients will respond favorably

4 The abstinence from sodium must be rigid Halfway measures are futile

5 The rice diet probably has as its main virtue a very low sodium content It is a good basic diet to start with when placing a patient on a low-sodium regimen Additions of foods of low-sodium content can then be made under well controlled conditions

6 The physician must be alert and well versed in the numerous sources of sodium other than foodstuffs which often vitiate the low-sodium diet including certain tooth pastes carbonated drinks and various medications

7 Many patients will not remain on the low sodium diets for protracted periods of time but, for permanent results the diet must be maintained

*General Medical Measures* —Regardless of whether hypertension produces symptoms in a given case and regardless of other forms of therapy the following measures should be incorporated into the regimen prescribed for patients with hypertension

1) Psychic factors should be controlled by adequate physical and mental relaxation including restricted hours of work rest periods before meals and at least 8 hours of sleep nightly Noncompetitive hobbies are desirable for many patients and frequent vacations of considerable length should be taken when possible

2) Any and all activities which produce sudden and considerable elevations of the blood pressure should be avoided—including swimming in cold water competitive sports activities which require great and sudden effort such as lifting, pushing, or squeezing The best form of physical exercise for the hypertensive patient is walking at a normal moderate pace

3) Weight reduction is always desirable in hypertensive patients who are obese It will not reduce the blood pressure in essential hypertension unless carried to the point of producing emaciation and debilitation, but it does improve the patient's ability to perform ordinary activities without dyspnea and discomfort The ideal weight for the average hypertensive is within the low normal range Weight reduction should be done slowly and not at the expense of restricting protein intake Despite current experimental work, there is no evidence that the restriction of cholesterol in the diet produces any modification in the course of clinical hypertension Fluid should not be restricted and, if edema occurs it should be controlled by the restriction of the sodium ion in the diet

4) Alcohol in moderation is probably advantageous because of its ability to produce generalized vasodilatation and to enable the patient to relax Excesses should not be permitted, however Tobacco in moderation has not been shown to be of any particular harm though it does provoke peripheral vasoconstriction and should be limited in quantity Beverages such as coffee and tea are permissible in moderation

### SYMPATHECTOMY

Sympathectomy is not curative in the sense of removing the cause since this is not known but it does produce considerable benefit in the relief of symptoms and appears to prolong the life of some hypertensive persons

The operative procedures have been varied and numerous, but have evolved during the past two decades from excisions of a relatively few sympathetic ganglia to almost complete bilateral sympathectomy Before this surgical therapeutic approach can be evaluated completely it will be necessary to study the postoperative course of a very large number of hypertensive patients for the duration of their lives a matter of probably a generation

of the patient are often beneficial since these patients often exhibit poor muscular development, undernutrition poor muscle tone and faulty posture In many instances the problem is purely psychosomatic

Drugs should not be administered to increase the blood pressure Sedation may be indicated for the highly nervous individual

*Prognosis* —The prognosis is excellent and the life expectancy of patients with constitutional hypotension is better than that of the general population

## ORTHOSTATIC HYPOTENSION

### (*Postural Hypotension*)

In most persons the rapid change of position from the recumbent to the erect may be accompanied at times by a feeling of giddiness or faintness due to the redistribution of blood in the vascular system as a result of the change of posture In patients with orthostatic hypotension this effect is accentuated so that faintness or actual syncope occur regularly upon such changes of position

*Etiology* —Change of position from the recumbent to the erect is accompanied by a redistribution of blood within the vascular system In the erect position the force of gravity increases the volume of blood in the lower portion of the body at the expense of the cerebral blood flow Cerebral anemia of any significant degree is prevented ordinarily by the intervention of vasoconstrictor reflexes and by a slight increase in the heart rate In the average individual only minor and transient changes of blood pressure occur with change of position In the patient with orthostatic hypotension the compensatory mechanisms are disturbed blood pressure changes are exaggerated and symptoms arise The impaired vasomotor response is frequently evident also by disturbances in sweating That the parasympathetic nerves are involved also is suggested by the depression of vagal response to alterations in blood pressure and to the administration of atropine Pooling of the blood in the dependent portions of the body is believed to take place in the venous side of the circulation

*Symptoms* —The following features are common to the majority of patients with orthostatic hypotension (1) a sharp decrease in both systolic and diastolic blood pressures with fainting or marked weakness upon assuming the erect position (2) diminished sweating which may be localized (3) failure of the pulse to accelerate sharply upon standing (4) accentuation of symptoms during hot weather (5) increased urinary output during recumbency Other features seen often in cases of orthostatic hypotension include (1) pallor, (2) youthful visage for actual age (3) tendency for B M R to be low (4) loss of libido with or without impotence (5) central nervous system disturbances and (6) blood urea elevated to the upper limits of normal

*Treatment* —Treatment of orthostatic hypotension consists of the administration of drugs which will prevent the fall of blood pressure to low levels when the patient stands The following drugs and dosage schedules are commonly employed

- Ephedrine sulphate 50 mg every 2 hours
- Benzedrine sulphate 20 mg upon awakening and 10 mg during the day
- Paredrine 40 mg

Doses are ordinarily given upon awakening and every two hours through the active portion of the day These drugs may have undesirable side reactions which must be taken into consideration when thinking of prolonged administration They should not be given after late afternoon since they may then interfere with nocturnal sleep

Sleeping with the head of the bed elevated from 6 to 18 inches on bed blocks is often helpful in ameliorating symptoms especially those which occur upon arising

The wearing of an abdominal belt may be of value in visceroptotic persons in preventing the pooling of blood in the splanchnic areas

## FUNCTIONAL OR VASOMOTOR DISTURBANCES

Vasomotor disturbances of the circulation are of two general types—those in which there is excessive vasoconstriction (vaso-

c) Sex Women develop atherosclerosis later in life than do men and the lesions are apt to be less severe

Because hypertensive patients (a) usually exhibit symptoms and signs arising from involvement of more than one organ, (b) frequently have one or more complicating diseases, and (c) frequently die following the onset of failure of more than one vital organ, the cause of death is often not clear However, it is generally accepted that 50 per cent of the patients with hypertension die of congestive heart failure 15 per cent die of coronary sclerosis, 15 per cent die of cerebrovascular accidents 8 per cent die of uremia, and the rest die of unrelated causes

According to Keith, the mortality among patients who have hypertension of grades I and II is 30 and 42 per cent respectively, within 4 years, among patients in group III, 78 per cent and in group IV 98 per cent

## HYPOTENSION

### (Low Blood Pressure)

The lower limits of normal for the blood pressure are less well defined than are the upper limits As a rule, the diagnosis of hypotension should not be made unless the patient exhibits a systolic pressure of not more than 100 mm Hg It is to be remembered that the normal systolic blood pressure at birth is between 50 and 60 *mm Hg* and though it rises gradually it does not exceed 100 mm until puberty

Hypotension may be discussed conveniently under three categories (1) symptomatic hypotension which is encountered in the course of a variety of diseases (2) constitutional hypotension permanently low blood pressure occurring in healthy adults and often familial in nature and (3) orthostatic hypotension the fall of blood pressure which occurs upon changing from the horizontal to the erect position

## SYMPTOMATIC HYPOTENSION

### (Secondary Hypotension)

Acute symptomatic hypotension often of a severe degree occurs in Addison s disease in Simmonds disease (hypophyseal cachexia) *in shock in circulatory collapse*, and during and after in any severe infectious diseases It is a common result of myocardial infarction or pulmonary embolism *A less severe form is seen in chronic debilitating* diseases such as pulmonary emphysema bronchial asthma and pulmonary tuberculosis It is seen almost always in *patients cachectic from any cause Hypotension* is one of the important diagnostic criteria for Addison s disease which should be suspected in the presence of persistent *hypotension below 80 mm Hg*

## CONSTITUTIONAL HYPOTENSION

### (Essential Hypotension)

About 3 per cent of healthy adults exhibit a low blood pressure which is usually symptomless and discovered accidentally when the pressure is taken in a physician s office It is wise to avoid emphasizing the fact that the blood pressure is low since many of these patients are neurasthenic and will utilize this unimportant finding as a basis for subsequent complaints

*Pathology* —A majority of patients with this type of hypotension conform to a constitutional type (1) thin asthenic habitus (2) small heart (3) visceroptosis (4) cold, clammy extremities (5) poor vasomotor reactions (6) sometimes postural hypotension (7) poor resistance to infection (8) a normally functioning cardiovascular system At autopsy they are shown to have small hypoplastic hearts

*Symptoms* —Many patients with this type of hypotension complain of lassitude fatigability vertigo inability to concentrate mentally palpitation coldness and sweating of the hands and feet general chilliness and headache It is almost never possible to associate these symptoms with any abnormality other than the presence of hypotension It is significant that this condition is much more common among females than among males This condition is frequently classified as neurocirculatory asthenia

*Treatment* —Medical treatment is nonspecific If the patient is aware of his hypotension he should be reassured concerning its significance Measures designed to improve the general psychic and physical status

of the patient are often beneficial since these patients often exhibit poor muscular development undernutrition poor muscle tone and faulty posture In many instances, the problem is purely psychosomatic

Drugs should not be administered to increase the blood pressure Sedation may be indicated for the highly nervous individual

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## ORTHOSTATIC HYPOTENSION
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The wearing of an abdominal belt may be of value in visceroptotic persons in preventing the pooling of blood in the splanchnic areas

## FUNCTIONAL OR VASOMOTOR DISTURBANCES

Vasomotor disturbances of the circulation are of two general types—those in which there is excessive vasoconstriction (vaso

spastic) and those in which there is excessive vasodilatation The commonest and most striking signs in the vasomotor disturbances are alterations in the color and temperature of the skin Such changes also occur in the organic peripheral vascular disease but are apt to be less striking and are usually accompanied by other signs and symptoms which *command attention*

The color of the skin is largely determined by the size and number of capillaries and venules the temperature depends upon the caliber of the arterioles When vasomotor reactions occur excessively and persistently, a disease state results Vasomotor disturbances may lead eventually to organic changes and to complications common to the organic arterial diseases

## VASOSPASTIC (VASOCONSTRICTOR) DISTURBANCES

A Raynaud s disease (primary or idiopathic Raynaud s syndrome)

B Raynaud s syndrome (secondary)

1 Traumatic vasospastic syndrome pneumatic hammer disease other types of repeated trauma as those resulting from the practice of stenography, piano playing, *etc* post traumatic or postoperative states with or without Sudeck s atrophy

2 Neurogenic secondary to c n s * disease spondylitis cervical rib neurovascular syndromes of the shoulder neuritis *etc*

3 Organic vascular disease secondary to arteriosclerosis obliterans thromboangiitis obliterans syphilitic arteritis embolism

4 Intoxications those caused by nicotine arsenic ergot (early) lead and other heavy metals

5 Miscellaneous diseases scleroderma lupus erythematosus paroxysmal hemoglobinuria, polycythemia vera

C Acrocyanosis

D Cutis Marmorata (early livedo reticularis)

E Vasospasm secondary to

1 *Lesions of c n s or peripheral nerves*

2 Thrombophlebitis

3 Acute arterial occlusion

4 Post traumatic osteoporosis

## RAYNAUD S DISEASE AND RAYNAUD S SYNDROME

(Raynaud s Phenomenon)

Raynaud s phenomenon consists of episodes of constriction of the smaller arteries and arterioles of the extremities resulting in intermittent changes in the color of the skin Classically there is pallor, cyanosis or both during the period of vasoconstriction, and usually intense rubor during the period of reactive hyperemia Raynaud's disease *refers to Raynaud s phenomenon occurring* without an associated and predisposing disease

The *criteria for making a diagnosis of* Raynaud s disease are (1) episodes of Raynaud s phenomenon excited by cold or emotion (2) bilateral involvement, (3) absence of gangrene beyond minimal cutaneous areas (4) absence of any associated, predisposing disease, (5) the history of symptoms for at least 2 years Secondary Raynaud s phenonemon occurs in association with and as a result of some primary organic *disease or some other specific stimulation* such as percussive trauma

The importance of the nosological distinction is as follows The term *Raynaud s phenomenon* may be used to describe succinctly the classical series of color and temperature changes which occur in the digits under a variety of circumstances and as a result of a variety of causes It is a descriptive term and does not imply recurrence nor does it suggest etiology When the phenomenon recurs as a result of some associated condition, it may then be called *Raynaud s syndrome* and may be used in conjunction with the term for the primary cause, as for example thromboangiitis obliterans with Raynaud s syndrome When the phenomenon is *recurrent and painstaking* investigation reveals a typical syndrome

* c n s —(central nervous system)

without apparent primary cause the condition may be classified as Raynaud's disease

## Etiology

The fundamental cause of Raynaud's syndrome is not known but certain stimuli are capable of initiating individual attacks

1) *Cold*—Cold is the principal factor in precipitating attacks of Raynaud's syndrome In the susceptible individual exposure to cold of a sufficient degree results in the development of vasospasm in the affected areas and this spasm is not relieved until the environmental temperature is increased The degree of cold necessary to produce an attack varies from individual to individual in highly susceptible individuals it may be between 56 and 70° F (13 3–21 1° C) Immersion of the hand in a basin of ice water, a common test for provoking vasospasm may not induce attacks but sufficient exposure of the body to cold air to cause generalized chilling will almost always induce the clinical phenomenon

Raynaud's syndrome is ordinarily more troublesome in winter than in summer and in colder temperate climates than in the tropics In severe cases however episodes may occur upon sudden drops in temperature in even warm climates

2) *Emotion*—Anger excitement and fear may precipitate attacks in susceptible individuals In some the effects of emotion aggravate the effect of cold in other patients emotional stimuli alone even in a warm environment are sufficient to precipitate attacks of vasospasm

3) *Traumatic Vasospastic Disease*—Traumatic vasospastic disease occurs in persons who use vibrating tools such as pneumatic hammers (pneumatic hammer disease) and also in those who do certain types of skilled work which subject the fingers to repeated though often mild trauma—for example stenographers concert pianists handball players and switchboard operators Vasospastic phenomena usually occur as long as the person persists in the occupation if this is not avoided the condition may become progressive and irreversible

4) *Occlusive Arterial Disease*—Raynaud's syndrome is relatively common during the early stages of thromboangiitis obliterans and may occur with arteriosclerosis obliterans As the organic disease progresses the vasospastic component usually diminishes

5) We have recently noted a high coincidence of the Raynaud's phenomenon and the hyperabduction syndrome of the shoulder girdle It may also accompany the cervical rib and scalenus anticus syndromes The exact interrelation of these conditions is as yet not completely understood

## Incidence

Raynaud's disease is predominantly a disease of women in a ratio of at least 3 to 1 In any instance of Raynaud's phenomenon in the male a primary disease is likely to be present This is not however always the case Raynaud's disease ordinarily appears during the early decades of life three-quarters of the patients manifest symptoms before the age of 40 years Raynaud's phenomenon appearing during later decades is usually a complication of organic vascular changes The sex and age incidence of secondary Raynaud's phenomenon is that of the primary or predisposing disease or trauma

## Pathology

The earlier stages of Raynaud's syndrome are purely vasomotor in nature and no structural changes are to be observed Later there are local thickenings in the walls of the smaller arteries and occlusions presumably due to repeated vasospastic insults Occlusion is unusual in vessels larger in diameter than those of the digits Eventually there is striking dilatation of the capillary bed as demonstrable in the capillaries of the nailfolds

Gangrene occurs only in advanced cases and is confined to limited cutaneous areas most commonly the tips of the digits Gangrene probably results from the combined effects of repeated vasospasm and organic occlusion It is not necessary for gangrene or trophic changes to be present to make the diagnosis as was suggested in Raynaud's original reports he apparently confused thromboangiitis obliterans with

what we now know as the true Raynaud's syndrome

During an attack, arteriolar spasm prevents blood from entering the capillaries During the stage of waxy pallor the capillaries are collapsed and empty, or interrupted, and the small amount of blood in them is stagnated The surface temperature of the involved area falls to approximate room temperature Later, there is a reflux of blood into the dilated capillaries from the venous side Stasis of this blood produces the deep cyanosis which often follows the stage of pallor With relief of the attack the arterioles open widely filling the capillaries and venules with oxygenated blood The involved areas become bright red and the surface temperature rises to above normal during this phase This may appear in a patchy distribution as the vessels open progressively

## Clinical

*Typical Clinical Picture* —Usually the patient is a young woman who has observed the classical color changes in her fingers upon exposure to cold Ordinarily the changes have developed gradually, but occasionally there has been a dramatic onset with the sudden appearance of an acute episode of pallor—the dead finger phenomenon' Early only a single digit may be involved but usually within a year or two the tips of the fingers in both hands become involved The color changes may consist only of pallor or cyanosis or both They usually include the phase of reactive hyperemia or rubor

Symptoms are worse during the cold season While pain is not prominent paresthesias (numbness burning tingling tightness pins and needles) are common During the attack the fingers are cold sensation may be impaired and there may be swelling which occasionally persists between attacks As the condition advances attacks become more frequent and more severe They may occur with the slightest cooling or upon the mildest emotional upset so that warm weather affords no relief

The fingers are involved in over 90 per cent of cases of Raynaud's disease the toes in slightly more than half the cases The nose, ears, and cheeks may be involved In the secondary form, the upper extremities are involved in the majority of cases The possibility that the Raynaud's phenomenon is a part of a drug reaction must be kept in mind during the taking of the history Skin eruptions and other stigmata of drug reactions should be sought Arthritis and edema occur in a few instances and should arouse a suspicion of lupus erythematosus and other collagenous diseases The occupational history is frequently important and may establish the diagnosis and etiology

## Physical Findings

Inspection of the extremities and particularly of the digits must be painstaking Trophic changes and early gangrene of the skin should be noted If possible an attack should be provoked and observed directly to determine the nature extent and duration of the changes which occur The effect of an emotional disturbance in provoking an attack should also be noted

It is important to identify the presence of any primary disease Occlusive arterial disease should be sought by palpation of the peripheral arteries by examination for postural color changes and by oscillometry Careful neurological examination must include testing of the reflexes The patient must be studied carefully for a possible neurovascular syndrome of the shoulder girdle In the presence of scleroderma the extent and duration of the sclerodermatous changes must be investigated carefully to determine whether the scleroderma is primary or secondary

## Course

The course of Raynaud's syndrome may range from very mild to severe In the former there is nonprogressive involvement of one or two digits occurring infrequently and only in response to severe cold or emotional upset In the latter there is steady progression involving not only the fingers and/or the toes but the hands or feet and even face as well there are also more frequent attacks precipitated by ever

TABLE 48.—DIFFERENTIAL DIAGNOSIS BETWEEN RAYNAUD'S DISEASE, ACROCYANOSIS, LIVEDO RETICULARIS, PERNIO AND ACROSCLERODERMA

| | *Raynaud's disease* | *Acrocyanosis* | *Livedo reticularis* | *Pernio (erythrocyanosis)* | *Acroscleroderma* |
|---|---|---|---|---|---|
| Age and sex | 70% of cases in girls and young women | 90% of cases in girls and young women | In either sex at any age | 70% of cases in young women | 85% of cases in young women |
| Type of color change | Mottled or diffuse white, blue, red | Diffuse blue | Mottled and reticulated red and blue | Localized red and blue | White, blue and red, mottled or diffuse |
| Location of symptoms | Fingers and toes, rarely nose and ears | Usually hands, occasionally feet | Usually legs, occasionally arms | On exposed surface, esp. legs | Hands and feet |
| Persistence of symptoms | Intermittent | Permanent | Permanent | Variable but aggravated in winter | Intermittent |
| Local symptoms | Burning pain if any | Usually none | Pain and coldness if any | Severe itching and burning | Stiffness and tension of skin |
| Effects of cold | Aggravates symptoms | Aggravates symptoms | Accentuates blueness | Increases redness | Symptoms aggravated |
| Effects of heat and vasodilatation | Decreases color changes greatly | Little change | Decreases blueness | Increases redness | Decreases color changes |
| Effects of posture and exercise | Little change | Elevation decreases cyanosis | Elevation or exercise decrease cyanosis | No change | No change |
| Necrosis and ulceration | Slight and limited if any | None | Only in severe cases | Commonly in severe cases | Frequent in advanced scleroderma |

TABLE 49.—THE DIFFERENTIAL DIAGNOSIS BETWEEN RAYNAUD'S DISEASE AND THE OCCLUSIVE ARTERIAL DISEASES, THROMBOANGIITIS OBLITERANS AND ARTERIOSCLEROSIS OBLITERANS

| | *Raynaud's Disease* | *Thromboangiitis Obliterans* | *Arteriosclerosis Obliterans* |
|---|---|---|---|
| Sex | More than 75% of cases are female | More than 95% of cases are male | More than 85% of cases are male |
| Age at onset (in years) | From puberty to 50 | From 20 to 40 | More than 50 |
| Raynaud's phenomenon | 100% of cases | About one third of cases | Uncommon, about 10% of cases |
| Postural color changes | Absent | Commonly present | Commonly present |
| Gangrene (if present) | Limited to small areas of skin | Minimal to extensive | Minimal to extensive |
| Involvement of upper limb | In almost all cases | In less than half of cases | Rare |
| Involvement of lower limb | Frequent but less so than in upper limb | In more than 95% of cases | In 100% of cases |
| Symmetry of involvement | Bilateral and symmetrical | Asymmetrical but usually bilateral | Asymmetrical but usually bilateral |
| Peripheral arterial pulsations | Palpable | Impaired or absent | Impaired or absent |
| Calcified arteries | Absent | Usually absent | Usually present |
| Superficial phlebitis | Unusual | Occurs in nearly one half of cases | Unusual |
| Acrosclerodema | May occur | Absent | Absent |

milder stimuli, and often the appearance of trophic changes and gangrene. Necrosis, ulceration and gangrene may occur in the absence of any demonstrable organic change in the vessels.

### Diagnosis

A typical attack of Raynaud's phenomenon is ordinarily sufficiently characteristic to establish the diagnosis. The differentiation between the Raynaud's disease and secondary Raynaud's syndrome may be more difficult. The demonstration of a causal primary disease may require observation of the patient over a period of time.

### Complications

Sclerodermatous changes, either primary or secondary to the Raynaud's phenomenon, may interfere with the use of the involved extremities, especially with the use of the fingers. Ulceration and gangrene of the tips of the digits cause discomfort, pain and loss of function. Only rarely does secondary infection become so severe as to require amputation of a digit. In some instances such infection involves the bones of the phalanges.

### Differential Diagnosis

The differential diagnosis between Raynaud's syndrome and the various vascular conditions with which it may be confused appears in the following tables.

### Treatment

Medical.—(1) *Protection Against Cold.*—The patient with Raynaud's syndrome must be protected carefully against cold. He should live in a warm climate, particularly during the winter. If outdoor activities cannot be avoided completely during cold weather, warm clothing is essential. Shoes should be sufficiently large to permit the patient to wear one or two pairs of woolen socks. Automobiles used by the patient should be heated. Fur lined gloves and lined galoshes should be worn out-of-doors. The patient should be instructed to maintain the warmth of the body, since cooling of the trunk, regardless of the temperature of the limbs, may cause reflex vasospasm in the extremities. The avoidance of cold will not prevent attacks entirely where emotional or other contributory factors persist.

2) *Tobacco.*—It is probably wiser to omit tobacco in most cases, since smoking causes vasoconstriction and repeated attacks of vasoconstriction lead to permanent structural damage to the smaller vessels. In patients with mild disease and whose habit of smoking is strongly established, temperature studies of the finger tips may be made to demonstrate how important a role smoking plays. It should be noted that smoking *per se* does not have the specific aggravating effect in Raynaud's syndrome which it has in thromboangiitis obliterans.

3) *Psychiatric.*—Many patients with Raynaud's syndrome have unstable vasomotor systems. Psychiatric evaluation and treatment of such patients is often of distinct value in treating Raynaud's phenomenon. Many are dreadfully afraid that their illness will result in the loss of digits or limbs. Reassurance is important. Many cases do not progress for decades. The patient may be warned, however, that his condition may ultimately become more disturbing and sympathectomy be necessary.

4) *Pain.*—Pain is usually not notable in Raynaud's syndrome, although discomfort may be intense during attacks of acute vasospasm. Simple warming of the body and of the hands will ordinarily relieve the average patient. Alcohol in the form of whiskey or brandy may be taken to hasten relief. Papaverine hydrochloride taken orally in doses of from 0.1 to 0.2 grams or Priscoline® 25 mg. may be prescribed every four hours during periods of exposure to cold. Papaverine may be given intravenously in doses of from .06 to .12 grams if necessary.

5) *Care of Involved Areas.*—Overheating an area of skin involved in vasospasm may produce serious burns because the circulation cannot carry off heat and metabolic wastes during the period of vasospasm. Warming of involved digits and limbs must be gradual and never excessive. Strong antiseptics must not be applied to superficial lesions of the ischemic tissues for fear of injury. The ulcers of Raynaud's syndrome heal best

when dry. If infected they may be soaked in *warm not hot* (temp 95° F) packs of normal saline or penicillin solution for an hour once or twice a day. Wet dressings must not be allowed to cool since chilling produces vasospasm.

6) *Adrenolytic and Sympatholytic Drugs*.—Tetraethylammonium chloride (Etamon) and bromide, dibenamine and Priscoline* have been used extensively during the past two years. Dibenamine has the disadvantage of requiring intravenous injection. The results of treatment with the tetraethylammonium ion have been disappointing because of the relatively fleeting action of the drug. The results reported with the use of Priscoline* are much more promising.

Priscoline* may be given orally, intramuscularly or intravenously. Its effect persists for from three to eight hours. It is usually administered in doses of from 25 to 75 mg at intervals of four hours. Larger doses are best avoided since they may produce acute attacks of hypotension. It appears to diminish (but not eliminate) attacks in some patients.

7) *Hormones*.—If Raynaud's syndrome first appears during pregnancy or is aggravated during menstruation or at the menopause, estrogenic therapy should be tried. Favorable results have been reported by L. V. Allen and his co-workers.

SURGICAL.—In mild and nonprogressive Raynaud's syndrome sympathectomy is not indicated. The patient should not be operated upon until observed over a period of months, preferably through one or more winters. If Raynaud's syndrome recurs each winter, especially if the attacks are severe, one may anticipate increasingly severe and more frequent attacks and eventually trophic changes and scleroderma. Sympathectomy is then indicated to reduce disability during the cold seasons and to prevent the development of ulceration and scleroderma. Residence in a warm climate may be tried in an effort to avoid surgery.

In selecting patients for sympathectomy, it is desirable first to try a course of one of the sympathetic blocking agents or perform sympathetic blocks by the injection of novocaine. It may be realized, however, that these preliminary procedures are not reliable indications of the value of sympathectomy, which should not be withheld from a patient because he does not respond favorably to them.

Sympathectomy for Raynaud's syndrome affecting the lower extremities is usually successful, but one cannot predict the benefit of sympathectomy to the upper extremities. This is unfortunate because of the predilection of Raynaud's syndrome for the upper limbs. Failure of sympathectomy is usually due to the failure to interrupt all sympathetic fibers leading to the involved limb. This may be because unknown pathways may carry sympathetic impulses. In all instances, sympathetic ganglionectomy and resection of the sympathetic trunks should be done.

The immediate improvement, including improved skin temperature of the involved areas, relief of subjective symptoms and healing of ulcers, may be short lived. The late results depend on the completeness of the operation, the stage of the disease at the time of operation and other factors not yet clear. No conclusion should be drawn until the patient has been observed postoperatively for several years. In late cases, especially those complicated by scleroderma, the results are rarely good.

## ACROCYANOSIS

Acrocyanosis is a condition characterized by painless and persistent coldness and cyanosis of the distal parts of the extremities. It is a benign condition, ordinarily innocuous except for mild discomfort and the annoyance of its appearance. Acrocyanosis is usually not progressive. It is important clinically to differentiate acrocyanosis from Raynaud's phenomenon.

*Etiology*.—The cause of acrocyanosis is not known. The color changes have been ascribed to dysfunction of the sympathetic nervous system, since patients exhibiting the phenomenon frequently have a family history of vasomotor instability. The work of Lewis and Landis, however, indicates that the essential fault is local.

*Pathology*.—The changes of acrocyanosis are not clearly known, but several observers have described distended and enlarged capil-

laries and venules. The capillaries are longer and wider than normal and become convoluted and tortuous. The physiological changes are also obscure. Elevation of the limb fails to reveal any evidence of obstruction to the venous drainage. The larger arteries are normal. These findings indicate that the fault must lie in the arterioles or in the capillaries and venules.

*Clinical.*—The usual patient has noted continuous coldness and cyanosis of the fingers and hands for a period of years. The toes and feet may have been involved to a lesser extent. Although the changes in color and temperature may be exaggerated during the winter months, they are present even in a warm environment. There are no episodes of blanching. Rubor is not usual though it may occur in a very warm environment. There may be some swelling of the involved parts and pain may occur in moderation. In the usual case there is no evidence of occlusive arterial disease. Marked sweating of the cool cyanotic extremities is very common and distressing.

*Course.*—The course of acrocyanosis is benign and nonprogressive. Trophic changes, scleroderma, and ulceration do not occur.

*Diagnosis.*—The diagnosis is ordinarily *not difficult. The nature, extent, and location* of the color changes are ordinarily typical and do not occur in the cyclic progression—pallor to cyanosis to rubor—so characteristic of Raynaud's phenomenon.

*Laboratory.*—Capillary microscopy can be done where facilities permit but is not ordinarily necessary.

*Treatment.*—Since acrocyanosis is innocuous and nonprogressive, treatment is ordinarily restricted to protection of the patient from the effects of cold. In severe cases, sympathectomy may be performed with the probability that the results will be somewhat better than those attained in Raynaud's syndrome.

*Prognosis.*—Since there are no sequellae or complications, the prognosis for the life of the tissues is good, but complete cures are not very common.

## ACUTE ARTERIAL VASOSPASM

### (Traumatic Arteriospasm, Segmental Arteriospasm)

Acute arteriospasm, involving an entire limb, or confined to a portion thereof, frequently follows gunshot wounds, fractures, and vascular injuries and may follow relatively minor trauma. It is present, to a degree, in all instances of organic arterial occlusion due *to thrombosis or embolism* and occurs occasionally in association with acute thrombophlebitis.

Arteriospasm may persist in a chronic form and be associated eventually with Sudeck's atrophy, a demineralization of the bone secondary to vasospasm.

*Etiology.*—The exact mechanism of development is not known, but acute arteriospasm is undoubtedly due to reflex sympathetic action. Trauma to the vessels themselves is not essential, since injury to skeletal or nerve by soft tissue structures may produce profound vasospastic effects.

*Pathology.*—In the walls of the involved vessels, there are no pathological changes due to arteriospasm *per se*. Thrombosis may occur within the lumina of the vessels if the vasospasm persists over a prolonged period of time.

*Clinical.*—The symptoms and signs of acute arteriospasm are similar to those of an acute or subacute organic *arterial occlusion*. The extent and the degree of the findings depend on the size and location of the involved vessels. When large arteries are involved, the clinical picture may be identical with that of sudden organic arterial occlusion. Unless the major vessel is explored, it is often difficult or impossible to determine whether there is an intravascular clot. Delayed recognition is not usually difficult if the spasm subsides.

Reflex vasospasm is of great importance in connection with organic occlusion of a major artery, since the spasm may involve *not only the segment of the artery* which is occluded but also the entire vessel, the arterial tree served by the major vessel, the collateral circulatory channels, or the major vessels of the entire limb. Recognition of the factor of spasm is of vital importance since it may often be relieved by measures

short of exploring the major artery and its relief may completely alter the clinical picture

*Treatment* —The treatment of acute arteriospasm of a reflex nature falls into three categories (1) treatment of the underlying disease or injury (2) treatment of organic arterial occlusion and (3) relief of the arteriospasm itself

Treatment of the primary condition consists of (1) immobilization of the affected limb (2) relief of pain (3) support of the systemic circulation to prevent failure (4) reflex heat (5) sympathetic blocks or sympathectomy and (6) corrective surgery for the original injury (if indicated)

When organic occlusion on the basis of thrombosis or embolism is present anticoagulants should be administered and consideration given to the possibility of surgical removal of the intravascular clot Relief of pain by immobilization of an injured extremity and by the administration of adequate amounts of codeine or morphine may in itself relieve milder degrees of arteriospasm Since the circulation to the extremity is impaired nothing should be done to increase the metabolism of the involved member The application of heat greater than that of normal body temperature is to be avoided

Measures directed toward the relief of the arteriospasm fall into three categories (1) the administration of drugs which relieve vasospasm (2) the blocking of the sympathetic trunks by the injection of novocaine and (3) sympathectomy The first and second methods should be given adequate trial before surgery is considered The time honored use of papaverine intravenously in doses of from 0 3 to 0 6 grams followed every four hours by the administration of from 0 6 to 12 grams orally may be supplemented by the use of the sympatholytic drugs Papaverine is even more striking in its effects when given into the artery supplying the affected limb The agent currently in favor is Priscoline® It may be given parenterally in doses of from 75 to 100 mg and followed up with oral doses at intervals of four hours If a salutory effect is not obtained in from four to eight hours a sympathetic block should be performed If this is successful additional blocks may be performed once or twice each day until the spasm is completely and permanently relieved Sympathectomy is necessary only when these measures fail but should not be postponed unduly for persistent arteriospasm is distinctly damaging to all tissues supplied by the affected vessel

## VASODILATOR DISTURBANCES—ERYTHERMALGIA

(Erythromelalgia)

Vasodilator disturbances are much less common than vasospastic conditions A well-defined syndrome is erythermalgia (erythromelalgia or Weir Mitchell's disease) which consists of the classical triad redness pain and an increase in the temperature of the involved area It does not include the painful red but *cold* extremity of the occlusive arterial disease called *erythralgia* or, preferably *painful rubor*

*Etiology* —The etiology of erythermalgia is not known It may occur as a primary or idiopathic condition or as a secondary symptom-complex of some other vascular disease as indicated in the following table

Etiological Classification of Erythermalgia (Erythromelalgia)

I Erythermalgia (Erythromelalgia)—primary
II Erythermalgia (Erythromelalgia)— secondary to
  A Polycythemia vera
  B Hypertension
  C Arteriosclerosis
  D Diabetes mellitus
  E Gout
  F Thromboangiitis obliterans
  G Organic neurologic disease
  H Trauma
  I Heavy metal poisoning—*e g* with thallium mercury arsenic
  J Miscellaneous—secondary to fever hyperthyroidism alcoholism neurocirculatory asthenia menopause

*Incidence* —Erythermalgia may appear in persons of any age though it most commonly appears in adults It is equally common among men and women

laries and venules. The capillaries are longer and wider than normal and become convoluted and tortuous. The physiological changes are also obscure. Elevation of the limb fails to reveal any evidence of obstruction to the venous drainage. The larger arteries are normal. These findings indicate that the fault must lie in the arterioles, or in the capillaries and venules.

*Clinical.*—The usual patient has noted continuous coldness and cyanosis of the fingers and hands for a period of years. The toes and feet may have been involved to a lesser extent. Although the changes in color and temperature may be exaggerated during the winter months, they are present even in a warm environment. There are no episodes of blanching. Rubor is not usual though it may occur in a very warm environment. There may be some swelling of the involved parts and pain may occur in moderation. In the usual case there is no evidence of occlusive arterial disease. Marked sweating of the cool cyanotic extremities is very common and distressing.

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*Laboratory.*—Capillary microscopy can be done where facilities permit but is not ordinarily necessary.

*Treatment.*—Since acrocyanosis is innocuous and nonprogressive, treatment is ordinarily restricted to protection of the patient from the effects of cold. In severe cases, sympathectomy may be performed with the probability that the results will be somewhat better than those attained in Raynaud's syndrome.

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or else is actually decreased. The pain of peripheral neuritis is not usually accompanied by rubor or by an elevation of skin temperature.

*Treatment.*—The treatment of erythermalgia is not uniformly successful. When it is secondary to some other condition, usually a vascular disease, an organic neurological disease, or heavy metal poisoning, treatment of the underlying condition is essential to successful management of the erythermalgia. Acetylsalicylic acid in doses as small as 10 grains (0.65 gms.) may bring about a surprising degree of relief for several days. Injections of epinephrine hydrochloride have also been reported as successful.

Some symptomatic relief may be obtained by avoiding the circumstances that cause vasodilatation. The patient may obtain relief by moving to a climate where temperatures are moderate. The patient should avoid exposing his feet to excessive warmth; he should not, for example, wear heavy socks or sit near an open fire, a stove, or a heater. The wearing of light weight socks or stockings and sandals or perforated shoes may be helpful. Treatment with roentgen rays or radium may also prove helpful but should be carried out only by an expert roentgenologist.

If these measures fail, it may very rarely be necessary to anesthetize the skin of the feet by cutting or crushing the peripheral nerves distributed to the involved areas. A logical method of treatment is the desensitization of the skin to warmth by immersing the extremities in water at 75° F. (23.8° C.) for 15 minutes twice daily for two or three days and then increasing the temperature of the water 1 or 2° for each two days of therapy. When distress is experienced, the temperature of the water should be reduced by several degrees for the subsequent treatment. There is no real evidence that this therapy is consistently helpful. Since it is sometimes impossible to be certain that peripheral neuritis may not be complicating the picture, large doses of Vitamin $B_1$ or Vitamin B complex are frequently administered.

*Prognosis.*—Complete recovery is unusual. Where the erythermalgia is secondary, the ultimate outcome depends on the primary disease.

## SYNDROMES PRODUCED BY CHANGES IN THE ENVIRONMENTAL TEMPERATURE

There are several well-defined syndromes other than Raynaud's syndrome in which changes in the environmental temperature cause signs and symptoms referable to the peripheral vascular system. Each of these syndromes is initiated by an abnormal reaction of the peripheral blood vessels to changes in environmental temperature, usually in the direction of excessive cold. The mechanisms producing the conditions are similar, but the manifestations are sufficiently different to warrant their separation into clinical entities.

Conditions which Result from Exposure to Marked Increases or Decreases in Environmental Temperatures

I. Sensitivity to cold and heat
II. Pernio
  A. Acute pernio (Acute chilblains)
  B. Chronic pernio (Chronic chilblains, erythrocyanosis)
III. Trench foot and immersion foot
IV. Frostbite

## SENSITIVITY TO COLD AND HEAT

Sensitivity to cold differs in its manifestations from chilblains and frostbite in that there is a systemic as well as a local reaction. The local lesion, occurring on the exposed portions of the body and less often on the mucous membranes as well, is typically urticarial and in severe cases may become angioneurotic edema. The systemic reaction is a typical vasovagal attack similar to that produced by the parenteral injection of histamine. The pulse rate is accelerated and the blood pressure falls; in severe attacks this results in syncope. Attacks are apt to be particularly severe if the cold sensitive patient has been exposed to an elevated temperature just before exposure to extreme cold.

The diagnosis of true sensitivity to cold can be confirmed in the office or clinic by

*Pathology*.—Information on pathology of erythermalgia is scanty. No consistent organic change has been reported.

*Physiology*.—The increased temperature of the involved skin is a constant finding. Distress appears regularly when the skin temperature is elevated above a critical point (ordinarily between 89.6 and 96.8° F. or 32 and 36° C.) and disappears when the temperature falls below that point.

Vasodilatation is the immediate cause of the increased temperature and the distress, but it is not the primary cause since distress can be produced by warming the skin to the critical temperature while the circulation has been brought to a halt by application of a tourniquet. Other manifestations of vasodilatation are increased amplitude of arterial pulsations, a subjective sense of throbbing, increased heat elimination, and increased oxygen content of the venous blood from the involved extremity. Hydrostatic pressure, though not alone the cause of the distress, does however play a role here since distress may be produced by increasing the intravascular pressure in a limb warmed to below the critical temperature and may be relieved by elevating a limb warmed to above the critical temperature. Pain may sometimes be relieved by direct pressure on the skin. It is apparent that the skin in erythermalgia is unusually sensitive to a degree of warmth tolerated with perfect comfort by the normal subject.

*Clinical*.—The usual complaint is of a burning distress in one or more extremities for a period of years. The hands and feet or localized portions of the extremities are usually involved. There is a relation between the distress and the circumstances in which the temperature of the skin is elevated (exercise, the wearing of heavy clothes, exposure to heat, *etc.*). Distress is often worse during the warm seasons. It is made worse by dependency and by elevation of the venous pressure.

The burning sensation persists for minutes or hours, but the patient may have learned that it can be relieved by exposing the involved areas to cold air or immersing them in cold water. Frequently he has learned to sleep with his feet uncovered, even in the winter.

If the patient has examined the involved area carefully, he will have noted that it becomes red or cyanotic and warm or hot to the touch during an attack. There may be a slight swelling of the area or even the whole limb, but trophic changes, gangrene, and ulcers do not occur in the primary form of the condition. When they do occur (in the condition's secondary form), they are caused by the underlying disease.

*Diagnosis*.—The diagnosis of erythermalgia is established when painful rubor is accompanied by an increased temperature of the involved skin. Distress, color changes, and elevated skin temperature occur when the limb, or the body, is warmed, or the involved limb is allowed to hang free. They are relieved by cooling the limb or elevating it. Examination of the involved areas during an attack is imperative for diagnosis. The skin temperature of that area is warmer than the corresponding area on the opposite limb. The arterial blood supply should be examined carefully by palpation of the arteries, by the elevation and dependency test, and by oscillometry. The systemic examination is important to rule out primary systemic disease.

Primary erythermalgia ordinarily involves both lower extremities and, rarely, the upper extremities as well. Secondary erythermalgia often involves only a single extremity. The diagnosis of the primary erythermalgia can be established only insofar as careful examination has failed to reveal an underlying cause.

*Laboratory*.—Temperature studies are invaluable in demonstrating the parallel relation between the increase in the skin temperature and the occurrence of rubor and distress. These studies should include demonstration that the distress is increased by dependency or increased venous pressure and relieved by elevation of the involved extremity. The blood should be examined carefully to rule out polycythemia vera.

*Differential Diagnosis*.—Primary erythermalgia must be differentiated from the occlusive arterial diseases, arteriosclerosis obliterans and thromboangiitis obliterans, in which paresthesias, burning pain, and rubor may occur. In these conditions, however, the temperature of the limb remains normal

or else is actually decreased. The pain of peripheral neuritis is not usually accompanied by rubor or by an elevation of skin temperature.

*Treatment.*—The treatment of erythermalgia is not uniformly successful. When it is secondary to some other condition, usually a vascular disease, an organic neurological disease or heavy metal poisoning, treatment of the underlying condition is essential to successful management of the erythermalgia. Acetylsalicylic acid in doses as small as 10 grains (0.65 gms.) may bring about a surprising degree of relief for several days. Injections of epinephrine hydrochloride have also been reported as successful.

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CONDITIONS WHICH RESULT FROM EXPOSURE TO MARKED INCREASES OR DECREASES IN ENVIRONMENTAL TEMPERATURES

I. Sensitivity to cold and heat
II. Pernio
  A. Acute pernio (Acute chilblain.)
  B. Chronic pernio (Chronic chilblains, erythrocyanosis.)
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## SENSITIVITY TO COLD AND HEAT

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The diagnosis of true sensitivity to cold can be confirmed in the office or clinic by

strapping an ice cube to the patient's forearm. An urticarial reaction will develop in 10 or 20 minutes. In patients insensitive to this test, a more violent reaction may be evoked by immersing the hand and arm into a container of water maintained at a temperature of from 12 to 14° C. (53.6° to 57.2° F.) or lower. The forearm test should always be tried before the immersion test, for, in extremely cold-sensitive patients, such exposure may produce syncopal attacks. Syncope, which in some cases, is believed to have caused drowning, has resulted from immersion of the entire body in cold water.

Some persons are similarly sensitive to heat; occasionally, a person is extremely sensitive to both heat and cold. Exercise, fever, or exposure to an excessively warm environment may induce attacks identical to those induced by exposure to cold. In such instances, exposure to a cool environment immediately before exposure to heat may aggravate the attacks.

*Treatment.*—Treatment of sensitivity to heat and cold is not satisfactory. Desensitization can sometimes be accomplished by daily exposing the hand to cold water. The temperature of the water should be lowered one degree each day. Histamine injected subcutaneously in progressively larger doses has also been used with occasional success. The value of antihistaminic drugs is being studied at present. Patients sensitive to cold should be warned against swimming in cold water, taking very cold showers, or indulging in cold foods or drinks.

## ACUTE AND CHRONIC PERNIO

### (Acute and Chronic Chilblains)

In acute pernio (acute chilblains) the patient complains of an itching, burning sensation of an exposed portion of the body, usually the hands or the feet, but occasionally the nose, the cheeks or the ears. The discomfort begins during exposure to cold but is aggravated by subsequent exposure to a warm environment or by bathing in warm water. The skin becomes somewhat red, oft-times mildly cyanotic, and there is usually slight edema in the involved areas. Small blebs may appear, but there is no severe urticarial reaction as in cold sensitivity. Resolution of the reaction is slow even if there is no further exposure to cold. Purpura often occurs; occasionally, a dermatitis. Brown pigmentation may remain permanently.

Repeated exposures to cold and dampness may result in chronic pernio (chronic chilblains). When this is the case, multiple small nodules may appear over the involved areas during the early weeks of the cold season. These nodules break down over the course of several weeks and become exquisitely painful ulcers, which persist through the cold season. The ulcers heal during late spring or early summer and leave permanently pigmented marks and disfiguring scars ranging in size from a pinhead to several centimeters in diameter. In advanced cases of chronic pernio the ulcers may not heal and may become disabling.

The normal skin temperatures of many persons who develop pernio is lower than the average person's. Their extremities are cold and frequently cyanotic. There may be unexplained mild ankle edema, and livedo reticularis is sometimes present.

The pathological picture in advanced chronic pernio is characteristic though not specific. There is angiitis with intimal proliferation, thickening of the arterial wall and perivascular infiltration, necrosis of the panniculus adiposus and a chronic inflammatory reaction of the subcutaneous tissues in which giant cells appear. The lesions, nodules, blebs, and superficial and deep ulcers may be present at the same time, and purpura and hyperpigmentation are not uncommon.

Chronic pernio must be differentiated from erythema induratum, erythema nodosum and nodular vasculitis.

*Treatment.*—There is no specific treatment for pernio. The patient must be protected against cold and dampness and after exposure to cold should not be exposed to heat greater than 85° F. Trauma to the skin should be avoided. Persons with acute attacks of chilblains should not have the exposed portion of their bodies rubbed with snow. Nor should strong antiseptics be applied to the involved areas. Mecholyl iontophoresis and intravenous typhoid vaccine have been used in chronic pernio but

with only moderate success Lumbar sympathectomy gives good immediate results but is disappointing as far as long range results are concerned The sympatholytic drugs are possibly worth a trial in the treatment of pernio

## TRENCH FOOT AND IMMERSION FOOT

Trench foot results from changes in the peripheral circulation and the tissues produced by exposure to cold and *dampness* There is ordinarily, a sterile mild inflammatory reaction, often there is a history of trauma Trench foot has been observed in all battles fought in severe, wet winter weather immersion foot is a product of modern amphibious warfare

*Etiology* —The following are the etiological factors (1) prolonged immobility of the legs (2) prolonged dependency of the legs (3) cold and dampness or prolonged soaking (4) want of opportunity to remove shoes or boots and socks, for long periods (5) constriction of the legs by boots or wearing apparel (6) improper nutrition (Protein and Vitamin B deficiencies are thought to be especially important)

*Pathology* —Trench foot is characterized by thrombosis of the vessels The soft tissues and bones of the affected part become necrotic there is intense scarring and fibrosis the subcutaneous fat is atrophic and phagocytized the muscles show atrophy much like that of Volkmann s contracture and the bones show a condition resembling Sudeck s atrophy Pathologically there is a close resemblance to frostbite

The earlier changes in immersion foot have not been well described but they appear to be similar to those in mild frostbite Later changes are often associated with gangrene or secondary infection Intimal thickening and medial fibrosis occur with some perivascular reaction Thrombosis however is not prominent The skeletal tissues atrophy and the the nerves especially toward the terminations show marked degeneration

*Clinical* —The patient with trench foot develops sensations of coldness dampness numbness and woodiness There is little or no pain while he remains exposed to cold Warmth however causes marked edema subcutaneous hemorrhages marked hyperemia and intense burning pain Gangrene may follow and though apt to be superficial is often very extensive Secondary infection is a constant risk until healing is complete

The clinical picture in immersion foot consists of three phases (1) the initial, or spastic ischemic phase, (2) the postimmersion or hyperemic phase and (3) the late vasospastic or secondary ischemic phase During immersion there is both direct and reflex vasoconstriction the feet are cold pale and cyanotic and the peripheral pulses are reduced or absent Edema appears as a result of dependency and aggravates the disturbances in the circulation Petechiae and shallow ulcers may appear Anesthesia is prominent

When the patient is placed in a warm environment the feet become swollen red and hot and the pulses begin bounding Swelling progresses and hemorrhagic blebs or ulcers and gangrene may appear Anesthesia and numbness may persist for a time but are eventually followed by intense and progressive burning paresthesias This phase may persist for weeks

In severe cases after weeks or months the feet become cold and cyanotic and pain stiffness and paresthesia are present Hyperhidrosis may then appear The late manifestations of the syndrome may reappear during cold weather for some years and prove incapacitating

## FROSTBITE

In frostbite severe and prolonged vasoconstriction causes ischemia of the tissues Thromboses in the smaller arteries contribute to the tissue damage Freezing of the tissue fluids occurs and intracellular fluids crystallize and rupture the cell membranes

The true freezing point of the skin is between −2 and 0° C (28 4 and 32° F) but freezing does not occur normally at this level because of the phenomenon of supercooling Freezing of the skin often occurs between −4 and −10° C (24 8 and 14° F) but occasionally it does not occur until the temperature has fallen to −20°

C. (−4° F.), or below. Freezing is encouraged by dampness, wind, circulatory stasis and anoxemia. Peripheral vascular disease, either vasospastic or occlusive, predisposes the skin to frostbite.

Frostbite may be classified, like burns, according to degree of severity. In first-degree frostbite, the outer layers of the skin are *involved in a white or yellow lesion* accompanied by numbness or paresthesia. Blistering or peeling does not occur. The application of mild warmth causes the normal color to return, but the affected part remains hypersensitive to cold for some time.

*In second-degree frostbite there is* blistering or peeling of the superficial layers of the skin, but the deeper layers of the skin and the subcutaneous tissues are undamaged. The tissues become firm and stiff.

When thawing occurs, reactive hyperemia spreads from the periphery to the center of the *involved area and a sensation of burning* pain is commonly experienced. Edema appears and is followed by blistering. Later the superficial skin peels, the result looks like necrosis or gangrene, but the subcutaneous tissues are normal.

Third- and fourth-degree frostbite are *analogous to third- and fourth-degree burns*, the former destroys the entire thickness of the skin, the latter involves the subcutaneous and deeper tissues. Necrosis and gangrene may lead to the loss of fingers or toes or of a hand or foot.

Persons who have been frostbitten are frequently hypersensitive to further exposure to extreme or even moderate cold and may be incapacitated upon such exposure.

*Treatment. — Prophylaxis.* —Persons exposed to severe cold *should wear loose*, light, warm, multilayered clothing. Outer clothes should be windproof. The feet *should be* kept oiled and dry and lesions of any sort treated carefully. Eskimo mukluk boots or at least loose, soft boots should be worn over two pairs of wool socks. Two pairs of gloves should be worn. Care must be taken to avoid unnecessary constriction of the extremities. Standing still for long periods is *undesirable when exposed to* extreme cold.

*Active Treatment.* — Mild (first-degree) *frostbite is best treated by* applying the warmth of the hand to the involved area. Heat above body temperature is unnecessary and undesirable.

In more severe degrees of frostbite, the patient should be kept in an environment maintained at "room temperature." The *skin must not be traumatized by* rubbing with snow or by walking. Warm drinks and alcoholic drinks will promote the peripheral circulation. The temperature of the frostbitten part should be raised to normal gradually. If severe pain occurs during the warming, the frostbitten parts may be kept *cool by means of an electric fan.* The rapid development of edema also indicates too rapid a rise in temperature. Sympathetic paravertebral blocks and sympathectomy have not proved of distinct value in the treatment of frostbite. The experimental and clinical studies by Lange and Boyd *suggest that all severely frostbitten patients* should receive heparin to minimize the development of thromboses in the small vessels involved. It is important that this be administered at the earliest possible time. Recent experience with frostbite incurred in the Korean war suggests that intravenous *infusions with procaine may be the* immediate treatment of choice. Surgical treatment of gangrenous and necrotic tissues should be delayed until all possible improvement has occurred, since the amount of devitalized tissue is often less than anticipated from the external appearance of the lesions.

## NEUROVASCULAR SYNDROMES OF THE SHOULDER GIRDLE

*Several types of anatomic derangements* of the shoulder girdle may be responsible for such neurovascular syndromes involving the arms as cervical rib syndrome, scalenus-anticus syndrome, costoclavicular syndrome and hyperabduction syndrome.

*Cervical-Rib and Scalenus Anticus Syndromes.* —The cervical rib syndrome occurs in the presence of extensions of the transverse processes of the 6th or 7th (occasionally of the 5th) cervical vertebra. Usually a supernumerary rib is present, but not always; it may be represented by a fibrous or

cartilaginous band The pressure of this structure on the subclavian artery and brachial plexus leads to coldness paresthesias, impaired circulation and occasionally gangrene of the fingers

The scalenus anticus muscle may produce a neurovascular syndrome by pressing the subclavian artery against the lower and middle trunks of the brachial plexus as they lie on a cervical rib Pinching may also occur between the anterior and the medial and minimal scalene muscles above their points of attachment to the first rib

Section of the scalenus-anticus muscle usually affords relief if the symptoms arise from the pinching of nerves and vessels between the first rib and the clavicle In the presence of a cervical rib such section is not so likely to afford relief

*Costoclavicular Syndrome* —In some persons holding the shoulders back and down or hyperextension of the neck pinches the vessels and the brachial plexus between the anterior surface of the first rib and the posterior surface of the clavicle Obliteration of the pulse may result Usually however unusual activity such as carrying a heavy pack is required to produce the syndrome Relief may be obtained by exercises that strengthen the shoulder muscles It is occasionally necessary to remove a rib or a section of a rib or to groove one of the ribs

*Hyperabduction Syndrome* —The hyperabduction syndrome is characterized by paresthesias numbness and tingling in the arms on holding them over the head for long periods of time It occurs most commonly in persons who sleep with the arms in hyperabduction and with the elbows flexed

Movement during sleep ordinarily relieves the discomfort Occasionally tingling loss of sensation swelling desquamation causalgia and even gangrene of the fingers may occur The syndrome is commonly seen as an occupational condition among aircraft workers painters and garage mechanics

## THE OCCLUSIVE ARTERIAL DISEASES

The occlusive arterial diseases are organic obliterative and obstructive conditions differing in etiology whose common denominator is eventual partial or complete arterial occlusion Occlusion may be insidious and slowly progressive as in uncomplicated arteriosclerosis obliterans or thromboangiitis obliterans or sudden and acute as in sudden arterial occlusion from thrombosis or embolism

**CLASSIFICATION OF THE OCCLUSIVE ARTERIAL DISEASES**

A Arteriosclerosis
  1 Generalized arteriosclerosis
  2 Arteriosclerosis obliterans
  3 Medial (Monckeberg's) arteriosclerosis
B Thromboangiitis obliterans (Buerger's disease)
C Simple arterial thrombosis
  1 Associated with infectious diseases
  2 Associated with blood dyscrasias
  3 Secondary to trauma or compression
  4 Idiopathic
D Arterial embolism
  1 Commonly from a thrombus (blood clot)
  2 Uncommonly bacterial neoplastic, fungus inorganic substances fat or air

## ARTERIOSCLEROSIS

### (Atheromatosis Atherosclerosis)

Arteriosclerosis is a degenerative process involving primarily the intima and sometimes the media of the walls of the arteries It is usually detectable during early or middle adult life and progresses insidiously Arteriosclerosis in the predominately elastic arteries the aorta and its branches is confined almost exclusively to the intima which becomes thickened and distorted as a result of the deposition of lipoid materials These deposits may become calcified or necrotic In severe cases the muscle fibers of the media may atrophy and be replaced with fibrous tissue Arteriosclerosis of the predominately muscular arteries the arterial trunks leading out into the extremities may involve the media without significant intimal change This is called Monckeberg's sclerosis

The term *atheromatosis* (atherosis) applies to the early stage of arteriosclerosis In this stage the lesions are relatively small isolated fatty subintimal plaques known as atheromata The term *atherosclerosis* is commonly applied to advanced degrees of atheromatosis When the arterioles are

involved, one speaks of *arteriolar sclerosis*

*Etiology*.—The etiology of arteriosclerosis is not known. Many theories have been advanced but only two warrant discussion here.

*Mechanical Theory*.—Since the time of Virchow, arteriosclerosis has been explained as a result of continuous trauma to the walls of the arteries due to the pulsating pressure of the circulating blood. The evidence is as follows:

1) Arteriosclerosis is generally associated with age but is clearly not related directly to age alone. Some persons have advanced lesions during the fourth decade of life or even earlier; others have no significant arteriosclerosis even at an advanced age. Both extremes, however, are exceptions to the rule. The earliest manifestations are ordinarily found in comparatively young adults, and the lesions tend to increase in size, number and extent as the years pass; the severest lesions are most frequently seen in persons of advanced age.

2) Severe degrees of arteriosclerosis often appear in several members of a single family and involve most extensively vessels of the same organ. This suggests that heredity may predispose to arteriosclerosis.

3) Although arteriosclerosis involves all parts of the vascular system, it commonly attacks arteries of a certain size, histological character and location—usually the elastic arteries, the aorta and its branches, the cerebral and the coronary arteries and the arterial trunks supplying the extremities.

4) Within the arteries most severely involved certain sites are usually especially affected. When the arteriosclerotic process is young, atheromata tend to develop in areas of maximum trauma: in the posterior wall of the aorta, in the site of insertion of the ductus arteriosus, in the bifurcation of the iliac arteries, and, if there is mitral valve disease, in the pulmonary circulation.

5) Arteriosclerosis obliterans is much more common in the lower than in the upper extremities. This is in keeping with the fact that arterial blood pressure is somewhat greater in the lower than in the upper extremities. The lower extremities are also subjected to more stress in most individuals.

6) Arteriosclerosis tends to develop earlier in life and to be more severe in patients with hypertension.

7) Atheromata are commonly found clustered around the mouths of the intercostal and other branches of the aorta and in similar locations where the stresses on the vessel walls are greater than elsewhere.

According to the mechanical theory, atheromata must be considered the result of a degenerative process in which lipoids are deposited secondarily and in a manner not necessarily related to any disturbance of lipoid metabolism.

*Metabolic Theory*.—Whether arteriosclerosis develops as a sequel to disturbed *cholesterol and lipid metabolism* within the organism is currently the subject of intensive experimental and clinical investigation. Here again the evidence is very convincing but we are plagued by a totally inadequate knowledge of the metabolism of the lipids. The evidence for this theory follows:

1) Atheromata of all ages and sizes contain large quantities of lipids in proportions similar to those found in the circulating plasma. This suggests that the deposits may result from nonselective infiltration from plasma to intima.

2) Lesions similar to the atherosclerotic lesions in man have been produced repeatedly and by numerous investigators in rabbits by the feeding of cholesterol or animal fat. What differences there are may be explained on the basis of species differences. Rabbits do not metabolize fats or cholesterol efficiently and when fed these substances develop marked hypercholesterolemia. Similar feeding experiments with other animals have failed to produce either hypercholesterolemia or arteriosclerotic lesions except when hypothyroidism has been produced by thiouracil.

3) Various disturbances of lipid metabolism in man which are accompanied by lipemia are frequently associated with severe atherosclerosis. Examples include idiopathic lipemia, xanthomatosis, diabetes mellitus and myxedema. Atherosclerosis was extremely common among diabetics during the pre-insulin era when high fat diets were commonly used in the treatment of diabetes mellitus. Atherosclerosis was

not common in Germany after World War I, when diets were comparatively low in fat

4) The levels of the plasma lipids including cholesterol cholesterol esters phospholipids and fatty acids appear to be elevated in many arteriosclerotics but owing to the variety of methods used in determining these substances in the blood to the considerable overlapping of the values obtained and to the great variation in the results as reported it is difficult to draw conclusions from the published data

5) One explanation of the deposition of cholesterol in the form of atheromatous plaques is that it passes from the blood plasma by direct filtration through the endothelium into the subendothelial tissues According to this view when the colloidal equilibrium of the plasma is disturbed inert cholesterol is able to diffuse into the subendothelial tissues It is engulfed by macrophages to produce the characteristic lipophages or cells engorged with fat Hueper has produced atherosis in animals by the intravenous injection of polyvinyl alcohol methyl cellulose pectin and acacia The lesions are histologically similar to those of atherosis in man and the localization is similar to that of cholesterol atherosis

6) The lipids in some persons blood are unusual in that the particles in suspension are particularly large visible by darkfield microscopy and separable by ultracentrifugation The size of the particles is not correlated with the absolute value of cholesterol in the blood Similar large particles have been observed in the plasmas of experimental animals after the administration of the substances used by Hueper to produce atherosis

Atherosclerosis may occur in persons predisposed to atherosis by the presence consistently or postprandially, of relatively large aggregates of lipoprotein components in the plasma By analytical ultracentrifugation Gofman has found four chief classes of lipoprotein components in sera

The class Sf10-20 was significantly elevated in patients with angina pectoris myocardial infarction nephrosis and in the majority of patients with hypothyroidism It appears that the type of lipoid material in the blood or the size of the chylomicrons may be more important than the actual amount of circulating lipids in the blood

7) Leary has explained atherosclerosis as follows Cholesterol is esterified in the liver by hepatic parenchymal cells During periods of overloading the lipid material accumulates in the parenchyma of the liver and damages the hepatic cells

These damaged cells are phagocytized by reticuloendothelial cells within the liver, which then become lipophages The lipophages enter the hepatic sinusoids and pass into the systemic circulation They adhere to the endothelium enter the subendothelial spaces and produce atheromata

To explain the localization of the atheromata Leary argues that the fibroblasts in the walls of the vessels are ordinarily able to remove cholesterol and that this ability is lost in certain vessels during adult life Gordon has carried this explanation a step further He states that the lipophages are less dense than other formed elements in the blood They move to the periphery of the moving blood stream and are forced against the endothelium by arterial pressure They enter the intima but are prevented from migrating beyond the internal elastic membrane which is impermeable to them In support of his view he points out that atheromata occur mainly in elastic arteries where the current is stronger and more intermittent than it is peripherally

8) Females tend to develop arteriosclerosis from five to ten years later than males which suggests that hormonal or metabolic differences may play some part in the development of the condition

## Pathology

The atheromatous process in early life consists of the development of the small intimal fatty plaques which arise from the deposition of cholesterol esters in the intercellular cement deep in the intima These plaques enlarge coalesce and gradually involve more superficial layers of the *intima* The process finally involves the surface endothelium and is visible in the lumen

True atherosclerosis usually appears in persons over 45 but varies widely in extent severity and localization Not only is fat



Fig 173 —Arteriosclerosis Hyaline degeneration involving entire thickness of wall of arterioles × 150 (Boyd Pathology of Internal Disease)

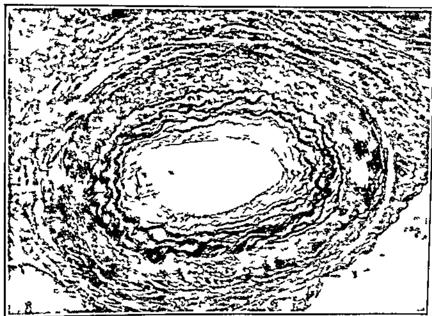


Fig 174 —Elastosis There is marked uniform thickening of the intima with reduplication of the internal elastic lamina From a case of essential hypertension (Elastic ti ue stain) × 150 (Boyd Pathology of Internal Disease)

laid down in the intercellular spaces of the intima but there is a fibrous reaction about it

Proliferation of the connective tissue elements in the intima is followed by hyaline degeneration, which produces the sclerotic intimal plaque In a given individual plaques of all sizes and degrees of development may be seen some of them simple atheromata others advanced atherosclerotic plaques Advanced lesions may become completely calcified or undergo necrosis and ulceration

### Pathological Physiology

Advanced arteriosclerosis may exist without clinical evidence of disease Symptoms arise as a result of impaired circulation and depend as much upon the location of the lesions as upon their number or stage of development In the smaller arteries the intimal thickening resulting from the atherosclerotic process and the secondary vasospasm may produce obstruction and occlusion In the larger arteries thrombosis produces occlusion

The importance of arteriosclerosis depends largely on its localization in terms of the organs involved Advanced arteriosclerosis is accompanied by atrophy of the capillary bed and subsequently by atrophy of the parenchyma of the organ involved

The high blood pressure accompanying advanced arteriosclerosis differs from that of essential hypertension in that only the systolic blood pressure is elevated

### Clinical Signs

In general the manifestations of arteriosclerosis are those described as senile changes—atrophy of the skin and its supporting tissues mental and physical impairment loss of memory for recent events increased irritability intolerance to cold and heat diminished resistance to infection delayed healing of wounds and predisposition to fractures (which heal slowly or not at all)

The localized clinical manifestations of arteriosclerosis are referable to the organ involved Cerebral arteriosclerosis may be manifested by the general signs of senility or by focal phenomena arising from involvement of major arteries Thrombosis aneurysm and hemorrhage complicate the arteriosclerotic process The results are ischemia from pressure and obstruction or infarction from complete occlusion In the end the brain substance degenerates and softens

Arteriosclerosis of the coronary arteries produces angina pectoris coronary insufficiency or coronary occlusion with myocardial infarction the last is commonly associated with thrombosis of a major coronary artery Myocardial failure with or without congestion is the result in patients who do not succumb to vascular occlusions or intercurrent diseases

Arteriosclerosis of the kidneys results in small contracted senile kidneys in which the circulation is impaired generally The clinical manifestations are polyuria nocturia and inability to concentrate the urine Edema does not develop but there is progressive impairment of renal function leading eventually, to uremia

### Diagnosis

The diagnosis of arteriosclerosis depends on the recognition of the stigmata of aging and on identification of the process as the cause of focal symptoms and signs occurring in the various vital organs Simple and readily performed bedside procedures are palpation of the peripheral arteries (the physician should remember to palpate the arteries of the feet) and examination of the fundi with the ophthalmoscope Roentgen examination of the major vessels may disclose the increased tortuosity characteristic of the disease and the deposition of calcium in the walls of the vessels Oscillometric readings of the extremities will indicate closure of or unusual lack of pulsation or elasticity in the major arteries but the cause must then be determined

### Laboratory Findings

In addition to the roentgen examination of the major vessels a variety of simple laboratory procedures are useful in making the diagnosis and determining the extent of the involvement of arteriosclerosis The



Fig 173 —Arteriosclerosis Hyaline degeneration involving entire thickness of wall of arterioles × 150 (Boyd Pathology of Internal Disease)

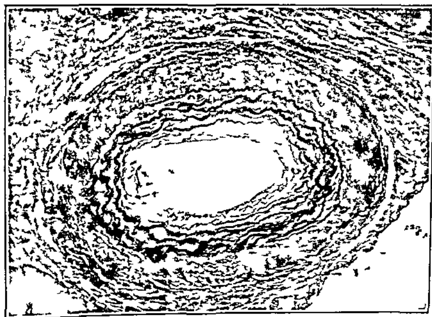


Fig 174 —Elastosis There is marked uniform thickening of the intima with reduplication of the internal elastic lamina From a case of essential hypertension (Elastic tissue stain) × 150 (Boyd Pathology of Internal Disease)

been necrosis or ulceration of the intima In the presence of such blood dyscrasias as hemophilia, thrombophilia and polycythemia thrombosis is likely to occur early in the development of atherosclerosis Postoperative and post traumatic thrombosis is very apt to occur in patients with atherosclerosis Any infectious disease or period of debility may be complicated by intravascular clotting in these patients

## INCIDENCE

Arteriosclerosis obliterans occurs predominantely in males over fifty

It is particularly likely to occur in patients with diabetes mellitus There is no definite evidence that it occurs with any greater severity among hypertensive persons than among others

sclerotic process is advanced the vessels may not be able to dilate significantly

The atheromatous plaques in the walls of the arteries project into the lumen as they enlarge adjacent plaques coalesce to form increasingly larger bodies Fibrous tissue is laid down around the plaques and the focal areas become calcified or necrotic Areas of degeneration may produce ragged, necrotic ulcers over which thrombi tend to form

The degree of involvement varies from vessel to vessel Progressive fibrosis of the intima results in an irregular thickening that reduces the diameter of the lumen Fibrosis progresses to involve both the media and the adventitia Calcification in the deeper layers of the intima may encircle the vessel completely

In the arterial trunks of the extremities

TABLE 50 —PATHOLOGICAL FEATURES WHICH DIFFERENTIATE ARTERIOSCLEROSIS OBLITERANS AND THROMBOANGIITIS OBLITERANS

| | *Arteriosclerosis Obliterans* | *Thromboangiitis Obliterans* |
|---|---|---|
| Thrombus | Irregularly deposited half moon-shaped layers of various ages Irregular and relatively acellular organization | Extensive organization containing endothelial cells and fibroblasts |
| Intima and subintima | Extensive atheromata formation usually eccentric Deposition of lipophages fat and cholesterol Often calcification | Inflammatory type of response Extensive proliferation of endothelium but no atheroma formation and consequently no deposition of fat cholesterol or calcium |
| Media | Irregular fibrosis and hyalinization often calcium deposition Thinning and appearance of moderate foci of lymphocytes and fibroblasts | Diffuse fibroblastic proliferation centering around vasa vasorum but muscular layers are preserved No calcium deposits |
| Adventitia | Irregular fibrosis Occasional foci of lymphocytes | Fibroblastic proliferation leads to periarterial fibrosis Marked endothelial proliferation of vasa vasorum |

## PATHOLOGY

Localized but widely distributed and extensive obstructive lesions involve the large and small arterial trunks When occlusion involves important arterial trunks or important collateral circulation or occurs suddenly ischemia of the tissues supplied by these vessels results The degree of ischemia may be increased by arteriolar constriction (from any cause—exposure to cold use of tobacco) or reduced as a result of vasodilatation as produced by heat or the use of vasodilator drugs If the arterio-

a distinctive type of arteriosclerosis Monckeberg s sclerosis not infrequently occurs In this condition there are degeneration and calcification of the media sometimes without significant intimal involvement The plate-like deposits tend to encircle the arteries and convert them into semi rigid tubes This process may extend from the iliac vessels down into the feet

The occurrence of hemorrhage around the vasa vasorum has been described in detail by Winternitz and others It is not clear whether such hemorrhage is primary or secondary

urinary sediment should be examined and the ability of the kidneys to concentrate urine determined The electrocardiogram is useful in assessing the status of the heart and the coronary circulation The hemoglobin concentration and erythrocyte count should be determined because of the common occurrence of secondary anemia, usually on a nutritional basis

### Treatment

There is no specific treatment of established value for the treatment of generalized arteriosclerosis The treatment of organs affected by arteriosclerosis is discussed in the chapters devoted to those organs General nonspecific measures are those which protect the patient against unnecessary strain and intercurrent disease infection particularly

*a*) Avoidance of exposure to excessive cold or heat Residence in a moderate climate is desirable when possible

*b*) Adequate but restricted diet Obesity *should be avoided weight reduction is* indicated when significant obesity exists Attention must be directed to assuring a well balanced diet, since patients of advanced age are prone to be careless about their eating habits Though some physicians advocate a low-cholesterol diet, this is so far based on inconclusive evidence *

*c*) Personal hygiene must be scrupulous The need for care in personal hygiene especially as to the feet increases as the resistance of the body is lessened yet the aged patient is often careless about such matters Instruction is not enough these patients require demonstration and supervision

*d*) Mental hygiene Mental deterioration and psychological maladjustment are common The elderly patient must be advised about his work and relaxation, his business and personal affairs He is prone to make mistakes and perform unexpected acts as a result of the gradual impairment of his memory and judgment

* According to Gofman and associates very low fat diets (50 gm ) with cholesterol restriction to 200 mg daily produce a reduction in the blood level of $S_f$ 10-20 molecules —Editor

### Prognosis

The prognosis must be guarded arteriosclerosis is inexorable and any one of a number of complications may ensue at any time—intravascular clotting hemorrhage vascular aneurysm and rupture, *etc* In general the chain of symptoms progresses gradually, regardless of the organs involved Death if not from intercurrent disease or trauma, occurs directly as the result of the arteriosclerosis It may however, occur as a result of acute coronary occlusion with myocardial infarction, myocardial weakness or congestive heart failure, renal insufficiency with uremia cerebrovascular accidents such as thrombosis, embolism and hemorrhage or the effects of acute arterial occlusion and gangrene The immediate cause of death from these complications is shock infection or toxemia Diabetes mellitus makes the prognosis considerably less favorable

## ARTERIOSCLEROSIS OBLITERANS

(Occlusive Arteriosclerosis Senile Gangrene, Diabetic Gangrene)

Arteriosclerosis obliterans commonly occurs in the extremities during the later decades of life It is characterized by progressive obliteration of the arterial lumina and frequently by episodes of acute and *complete occlusion It is the most common* of the peripheral occlusive arterial diseases and accounts for well over 50 per cent of such cases Its cause and development and the pathological picture presented are similar to those of arteriosclerosis elsewhere in the body

### Etiology

Age and the burden of living play important parts in the progress of the pathological changes in the vessels Disturbed lipid metabolism (hyperlipemia) is now known to be a potent factor in the production of atheromata

Thrombosis may occur as a complication in early or advanced arteriosclerosis The numerous (and ill understood) factors regulating intravascular clotting determine this event It occurs more readily in the presence of small atheromata when there has

heart disease renal disease or thyroid deficiency

7) *Condition of the Arteries* —Palpation of the arteries may disclose nodulation or hardening due to calcification Resistance to compression is usually most readily apparent in the radial arteries Increased tortuosity is usually visible in the brachial arteries

8) *Ulcers* —The ulcers of arteriosclerosis obliterans are due to ischemia and are commonly precipitated by trauma or by a splitting of the skin through fungus infection The ulcers tend to occur on the toes or between them on the heels and on the anterior tibial surfaces

Unless infected they tend to be dry Secondary infection by bacteria or fungi is very common The ulcers tend to extend themselves by undermining the surrounding skin margin and are not infrequently covered by a black eschar

9) *Gangrene* —Gangrene due to arteriosclerosis obliterans may involve a minute focal area or a large portion of the affected limb It depends on the size and location of the occluded vessel and on such other factors as the nutritional state of the patient the adequacy of the collateral blood supply and the occurrence of trauma and secondary infection Closure of even such major arterial trunks as the iliac arteries may not lead to gangrene if the collateral circulation is adequate Gangrene may involve a minute area and spread progressively or involve an entire digit or a large portion of an extremity (as a result of the occlusion of a major vessel for which no adequate collateral circulation exists) The pain is variable If infection does not supervene the area may remain dry and become mummified

## Special Examination

Certain tests are useful in the study of impaired peripheral arterial circulation regardless of etiology

1) *Oscillometry* —Oscillometry is valuable in determining the patency of major arteries and the level of occlusion

Oscillometry may give normal readings when major vessels are patent but subsidiary vessels at the same level are occluded it may show adequate circulation when palpation fails to do so because of the aberrant location of the major vessels Oscillometry is valuable when it discloses a distinct difference in the degree of pulsation at the same level in opposite limbs It is not of value in determining the adequacy of collateral circulation Oscillometry should always be performed in a warm room since chilling may produce vasospasm and diminished pulsations

2) *Surface temperature Studies* —The surface temperatures of two extremities may be compared clinically with satisfactory accuracy by palpation it is occasionally advisable to determine the skin temperature more accurately by means of a thermocouple For exact results this must be done in an environmental temperature that is kept constant

3) *Reflex vasodilatation Test* —To determine the potential ability of the vessels of a limb to dilate reflex vasodilatation or sympathetic block may be used The simplest test involves the application of heat to the arms or the trunk Where vasospasm is intense and unresponsive to simple measures the sympathetic nerves may be blocked by spinal anesthesia paravertebral block or local nerve block

4) *Claudication Tests* —It is helpful in assessing the degree of functional impairment and estimating improvement under therapy to have the patient climb stairs or walk a certain distance at a fixed pace

Similar and perhaps more accurate results can be obtained with an ergometer or by means of the forced contraction of the muscles through faradic stimulation (Landis) It is important in such studies to be certain that the pace of the patient is constant from test to test

## Laboratory Findings

1) *X rays* —Soft tissue roentgenograms of the leg and thigh and sometimes of the pelvis the lumbar region and the abdomen may help demonstrate calcified vessels Calcifications can be demonstrated in about two-thirds of the men and one-third of the women with arteriosclerosis obliterans Cal-

Thrombosis is the usual result of the vascular changes of arteriosclerosis obliterans It almost always occurs in advanced sclerosis and is not uncommon even in mild arteriosclerosis Thrombosis is probably related to alterations in the coagulation mechanism of the blood as well as to changes in the blood flow and to structural alterations in the walls of the vessels Organization and recanalization are ordinarily prominent in arteriosclerosis obliterans

Aneurysms of the peripheral arteries are relatively common late sequellæ of arteriosclerosis obliterans The popliteal and the innominate arteries are common sites Aneurysms may be saccular or dissecting and false aneurysms are not rare

## Clinical Signs

The signs and symptoms most commonly produced by arteriosclerosis obliterans are

1) *Pain* —Pain is the most common presenting symptom it may simulate that of arthralgia, neuritis *etc* but is most commonly that of intermittent claudication Pain at rest is common, and ischemic neuritis frequently occurs

Intermittent claudication is a syndrome caused by the relative ischemia of muscle groups upon activity It is analagous to angina pectoris It is characterized by extreme fatigue and tightness or cramping pain pain increased by walking a limited distance and relieved by resting for a short period Resumption of activity causes the pain to return

Claudication occurs most commonly in the muscles of the calf but also occurs in the muscles of the feet and thighs and occasionally in the muscles of the arms as among laborers Claudication is sometimes worse during cold weather and is aggravated by walking rapidly or up a grade of even modest degree The pain of intermittent claudication is characteristic (*a*) it is produced by exercise (*b*) it appears regularly and promptly after a given degree of exercise and (*c*) it is relieved by rest Claudication may be effected in a normal extremity by binding a tourniquet tightly around the proximal portion so as to occlude the arterial blood supply and then having the patient exercise the limb

Rest pain, which occurs while the patient is in bed, is like a cramp or dull ache It is presumably due to relative ischemia ischemia resulting from stagnation of the blood and the consequent impairment of nutrition and accumulation of metabolic wastes Severe neuritic pain may arise as a result of ischemia of the nerves

2) *Sensory Disturbances* —Patients with arteriosclerosis obliterans commonly complain of coldness numbness and tingling in the hands and feet and of difficulty in warming the extremities The surface temperatures are very often reduced even when the patient is not conscious of coldness In instances of arterial occlusion the surface temperature is usually distinctly lowered until the collateral circulation has become adequate skin temperature may remain depressed because of vasospasm Vibratory sensation may be impaired

3) *Trophic Changes* —Ischemia of the limb leads to trophic changes as a result of impaired nutrition There is atrophy of the skin and of the nails the latter becoming brittle thickened and deformed With advanced atrophy of the skin sweating is reduced and the growth of hair impaired Muscle atrophy is a prominent sign of chronically impaired peripheral circulation and produces the characteristic *pipe stem* legs of the aged

4) *Postural Color Changes* —The occurrence of extreme pallor upon the elevation of an extremity and of striking rubor often accompanied or followed by cyanosis upon dependency is definite evidence of arterial insufficiency Often pallor or rubor predominates but one is rarely present in the total absence of the other The time required for the feet to become distinctly pale upon elevation and brightly flushed upon dependency is useful in estimating the patency of the arterial supply

5) *Edema* —Since the venous pressure is not increased by arteriosclerosis obliterans edema does not occur on this basis alone If edema does exist a careful search must be made for local or systemic complication venous impairment nutritional disturbance

heart disease renal disease or thyroid deficiency

7) *Condition of the Arteries* —Palpation of the arteries may disclose nodulation or hardening due to calcification Resistance to compression is usually most readily apparent in the radial arteries Increased tortuosity is usually visible in the brachial arteries

8) *Ulcers* —The ulcers of arteriosclerosis obliterans are due to ischemia and are commonly precipitated by trauma or by a splitting of the skin through fungus infection The ulcers tend to occur on the toes or between them on the heels and on the anterior tibial surfaces

Unless infected they tend to be dry Secondary infection by bacteria or fungi is very common The ulcers tend to extend themselves by undermining the surrounding skin margin and are not infrequently covered by a black eschar

9) *Gangrene* —Gangrene due to arteriosclerosis obliterans may involve a minute focal area or a large portion of the affected limb It depends on the size and location of the occluded vessel and on such other factors as the nutritional state of the patient the adequacy of the collateral blood supply and the occurrence of trauma and secondary infection Closure of even such major arterial trunks as the iliac arteries may not lead to gangrene if the collateral circulation is adequate Gangrene may involve a minute area and spread progressively or involve an entire digit or a large portion of an extremity (as a result of the occlusion of a major vessel for which no adequate collateral circulation exists) The pain is variable If infection does not supervene the area may remain dry and become mummified

## Special Examination

Certain tests are useful in the study of impaired peripheral arterial circulation regardless of etiology

1) *Oscillometry* —Oscillometry is valuable in determining the patency of major arteries and the level of occlusion

Oscillometry may give normal readings when major vessels are patent but subsidiary vessels at the same level are occluded it may show adequate circulation when palpation fails to do so because of the aberrant location of the major vessels Oscillometry is valuable when it discloses a distinct difference in the degree of pulsation at the same level in opposite limbs It is not of value in determining the adequacy of collateral circulation Oscillometry should always be performed in a warm room since chilling may produce vasospasm and diminished pulsations

2) *Surface temperature Studies* —The surface temperatures of two extremities may be compared clinically with satisfactory accuracy by palpation it is occasionally advisable to determine the skin temperature more accurately by means of a thermocouple For exact results this must be done in an environmental temperature that is kept constant

3) *Reflex vasodilatation Test* —To determine the potential ability of the vessels of a limb to dilate reflex vasodilatation or sympathetic block may be used The simplest test involves the application of heat to the arms or the trunk Where vasospasm is intense and unresponsive to simple measures the sympathetic nerves may be blocked by spinal anesthesia paravertebral block or local nerve block

4) *Claudication Tests* —It is helpful in assessing the degree of functional impairment and estimating improvement under therapy, to have the patient climb stairs or walk a certain distance at a fixed pace

Similar and perhaps more accurate results can be obtained with an ergometer or by means of the forced contraction of the muscles through faradic stimulation (Landis) It is important in such studies to be certain that the pace of the patient is constant from test to test

## Laboratory Findings

1) *X-rays* —Soft tissue roentgenograms of the leg and thigh and sometimes of the pelvis the lumbar region and the abdomen may help demonstrate calcified vessels Calcifications can be demonstrated in about two-thirds of the men and one third of the women with arteriosclerosis obliterans Cal

Thrombosis is the usual result of the vascular changes of arteriosclerosis obliterans It almost always occurs in advanced sclerosis and is not uncommon even in mild arteriosclerosis Thrombosis is probably related to alterations in the coagulation mechanism of the blood as well as to changes in the blood flow and to structural alterations in the walls of the vessels Organization and recanalization are ordinarily prominent in arteriosclerosis obliterans

Aneurysms of the peripheral arteries are relatively common late sequellæ of arteriosclerosis obliterans The popliteal and the innominate arteries are common sites Aneurysms may be saccular or dissecting and false aneurysms are not rare

## Clinical Signs

The signs and symptoms most commonly produced by arteriosclerosis obliterans are

1) *Pain* —Pain is the most common presenting symptom it may simulate that of arthralgia neuritis, *etc*, but is most commonly that of intermittent claudication Pain at rest is common and ischemic neuritis frequently occurs

Intermittent claudication is a syndrome caused by the relative ischemia of muscle groups upon activity It is analagous to angina pectoris It is characterized by extreme fatigue and tightness or cramping pain pain increased by walking a limited distance and relieved by resting for a short period Resumption of activity causes the pain to return

Claudication occurs most commonly in the muscles of the calf but also occurs in the muscles of the feet and thighs and occasionally in the muscles of the arms as among laborers Claudication is sometimes worse during cold weather and is aggravated by walking rapidly or up a grade of even modest degree The pain of intermittent claudication is characteristic (*a*) it is produced by exercise (*b*) it appears regularly and promptly after a given degree of exercise and (*c*) it is relieved by rest Claudication may be effected in a normal extremity by binding a tourniquet tightly around the proximal portion so as to occlude the arterial blood supply and then having the patient exercise the limb

Rest pain which occurs while the patient is in bed is like a cramp or dull ache It is presumably due to relative ischemia ischemia resulting from stagnation of the blood and the consequent impairment of nutrition and accumulation of metabolic wastes Severe neuritic pain may arise as a result of ischemia of the nerves

2) *Sensory Disturbances* —Patients with arteriosclerosis obliterans commonly complain of coldness numbness and tingling in the hands and feet and of difficulty in warming the extremities The surface temperatures are very often reduced even when the patient is not conscious of coldness In instances of arterial occlusion the surface temperature is usually distinctly lowered until the collateral circulation has become adequate skin temperature may remain depressed because of vasospasm Vibratory sensation may be impaired

3) *Trophic Changes* —Ischemia of the limb leads to trophic changes as a result of impaired nutrition There is atrophy of the skin and of the nails the latter becoming brittle thickened, and deformed With advanced atrophy of the skin sweating is reduced and the growth of hair impaired Muscle atrophy is a prominent sign of chronically impaired peripheral circulation and produces the characteristic pipe stem legs of the aged

4) *Postural Color Changes* —The occurrence of extreme pallor upon the elevation of an extremity and of striking rubor often accompanied or followed by cyanosis upon dependency is definite evidence of arterial insufficiency Often pallor or rubor predominates but one is rarely present in the total absence of the other The time required for the feet to become distinctly pale upon elevation and brightly flushed upon dependency is useful in estimating the patency of the arterial supply

5) *Edema* —Since the venous pressure is not increased by arteriosclerosis obliterans edema does not occur on this basis alone If edema does exist a careful search must be made for local or systemic complication venous impairment nutritional disturbance

### Prognosis

Arteriosclerosis obliterans is a progressive degenerative disease hence the prognosis must always be guarded Owing to the development of collateral circulation however the outlook in many cases is much better than would be supposed

Many factors play a role in determining the eventual outcome the extent of the occlusive process the speed with which it develops the stage of the disease at which treatment is started the adequacy of the collateral circulation the presence or absence of trauma the age of the patient and the presence or absence of diabetes and other complicating diseases As a rule however, the life expectancy of patients with arteriosclerosis obliterans is reduced Death usually occurs as a result of coronary occlusion cerebrovascular accident mesenteric thrombosis or bronchopneumonia The mortality rate after amputation formerly relatively high has been markedly reduced by modern surgical techniques and antibiotic and chemotherapeutic drugs

### Basic Principles of Treatment of Arteriosclerosis Obliterans

1 Protection of tissues whose blood supply has been impaired
2 Prevention of vasoconstriction and production and maintenance of vasodilatation
3 Relief of pain
4 Use of local measures to heal ulcers and limit gangrene
5 Prevention of progress of disease
6 Amputation the final resort

### Plan of Treatment Involving these Principles

I *Procedures applying to all cases*
- A Education of patient on care and protection of feet
- B Institution of low fat low-cholesterol diet in instances of hyperlipemia
- C Reduction of weight if patient is obese
- D Careful control of patients with diabetes mellitus
- E Control of polycythemia if present
- F Strict limitation of tobacco

II *Additional measures in cases with intermittent claudication only*
- A Warm bath daily (temp 95–100° F or 35–37 7° C ) followed by anointing of feet with oil or lanolin
- B Postural exercises three times daily (Buerger s exercises)
- C Use of vasodilator substances (*e g* alcoholic beverages, Priscoline* Roniacol*)
- D Sympathetic block (or sympathectomy) in certain instances
- E Use of reflex heat

III *Additional measures in cases with ischemic neuritis or rest pain but without ulcers or gangrene*
- A Hospitalization and absolute bed rest
- B Use of an oscillating bed if available
- C Maintenance of temperature of room at 80–85° F (26 6 to 29 4° C )
- D Application of reflex heat to abdomen and trunk
- E Administration of alcohol by mouth b i d or t i d
- F Prescription of analgesics as necessary for relief of pain
- G Trial of sympathetic blocking agents
- H Sympathetic lumbar block
- I Sympathectomy in selected cases

IV *Additional measures in cases with ulcers or superficial gangrene*
- A Hospitalization at absolute bed rest in a warm room
- B Use of an oscillating bed if available
- C Warm soakings with normal saline solution
- D Local application to infected ulcers or gangrene of sulphonamides or antibiotics in appropriate solution or ointment
- F Local application of powdered erythrocytes to clean healing ulcers

cification, whether localized and patchy or regularly distributed and confluent, does not prove obliteration of the lumina of the arteries but may support such a diagnosis made on clinical grounds Roentgenograms of the feet may demonstrate osteoporosis Arteriography is not often necessary it may be useful occasionally in demonstrating the extent of the process and in locating sites of obstruction when surgical intervention is contemplated

2) *Blood sugar Determination* —The common occurrence of diabetes mellitus in patients with arteriosclerosis requires that all patients with arteriosclerosis have a careful urinalysis and a blood sugar determination A glucose tolerance test is desirable occasionally

5) *Electrocardiograms* —Because of the common coexistence of coronary atherosclerosis an electrocardiogram should be obtained

## Diagnosis

To make the diagnosis of arteriosclerosis obliterans it is necessary to demonstrate objectively the presence of occlusive arterial disease This is done by demonstrating absent or grossly impaired peripheral pulses and is supported by demonstrating abnormal postural color changes typical intermittent claudication and the presence of ulcers or gangrene The age of the patient is an important consideration 95 per cent of the patients 50 or older with occlusive arterial disease have arteriosclerosis obliterans The

TABLE 51 —DIFFERENTIAL DIAGNOSIS BETWEEN ARTERIOSCLEROSIS OBLITERANS AND THROMBOANGIITIS OBLITERANS

| | *Arteriosclerosis Obliterans* | *Thromboangiitis Obliterans* |
|---|---|---|
| Age at onset of symptoms | Usually over 40 years | Usually under 50 years |
| Sex | 75% of serious cases in the male | More than 95% of cases in the male |
| Involvement of upper limbs | Rare | In less than ⅓ of cases |
| Superficial phlebitis | Absent | In somewhat less than half of cases |
| Calcification of arteries | Present in about two-thirds of patients | Absent |
| Hypertension | Present in at least a third of cases | Unusual in early years of disease |
| Diabetes mellitus | Present in one-fifth of all cases | Unusual in early years of disease |
| Plasma lipids | Hyperlipemia common | Usually normal |

3) *Plasma lipid Studies* —Hyperlipemia is exceedingly common in patients with arteriosclerosis and should be studied in instances where the diagnosis is in doubt

4) *Hematocrit Determinations* — Polycythemia is not unusual in patients with arteriosclerosis obliterans and predisposes to intravascular clotting All patients with arteriosclerosis obliterans should have a careful blood count and hematocrit determination

If it is suspected that the coagulation mechanism is disturbed the coagulation time and the prothrombin time should be studied

differential diagnosis between arteriosclerosis obliterans and thromboangiitis obliterans is often difficult in men between 40 and 50 years of age Nearly all instances of occlusive arterial disease in women are arteriosclerotic although the average age of onset of symptoms is nearly a decade later than in men X ray evidence of calcification favors though its absence does not exclude the diagnosis of arteriosclerosis obliterans Evidence of generalized arteriosclerosis or hyperlipemia also favors such a diagnosis

*Differential Diagnosis* —*See* accompanying table

### Prognosis

Arteriosclerosis obliterans is a progressive, degenerative disease; hence the prognosis must always be guarded. Owing to the development of collateral circulation, however, the outlook in many cases is much better than would be supposed.

Many factors play a role in determining the eventual outcome: the extent of the occlusive process, the speed with which it develops, the stage of the disease at which treatment is started, the adequacy of the collateral circulation, the presence or absence of trauma, the age of the patient, and the presence or absence of diabetes and other complicating diseases. As a rule, however, the life expectancy of patients with arteriosclerosis obliterans is reduced. Death usually occurs as a result of coronary occlusion, cerebrovascular accident, mesenteric thrombosis, or bronchopneumonia. The mortality rate after amputation, formerly relatively high, has been markedly reduced by modern surgical techniques and antibiotic and chemotherapeutic drugs.

### Basic Principles of Treatment of Arteriosclerosis Obliterans

1. Protection of tissues whose blood supply has been impaired.
2. Prevention of vasoconstriction and production and maintenance of vasodilatation.
3. Relief of pain.
4. Use of local measures to heal ulcers and limit gangrene.
5. Prevention of progress of disease.
6. Amputation, the final resort.

### Plan of Treatment Involving These Principles

I. *Procedures applying to all cases*
   A. Education of patient on care and protection of feet.
   B. Institution of low fat, low-cholesterol diet in instances of hyperlipemia.
   C. Reduction of weight if patient is obese.
   D. Careful control of patients with diabetes mellitus.
   E. Control of polycythemia if present.
   F. Strict limitation of tobacco.

II. *Additional measures in cases with intermittent claudication only*
   A. Warm bath daily (temp. 95–100° F or 35–37.7° C) followed by anointing of feet with oil or lanolin.
   B. Postural exercises three times daily (Buerger's exercises).
   C. Use of vasodilator substances (e.g., alcoholic beverages, Priscoline®, Roniacol®).
   D. Sympathetic block (or sympathectomy) in certain instances.
   E. Use of reflex heat.

III. *Additional measures in cases with ischemic neuritis or rest pain but without ulcers or gangrene*
   A. Hospitalization and absolute bed rest.
   B. Use of an oscillating bed if available.
   C. Maintenance of temperature of room at 80–85° F (26.6 to 29.4° C).
   D. Application of reflex heat to abdomen and trunk.
   E. Administration of alcohol by mouth b.i.d. or t.i.d.
   F. Prescription of analgesics as necessary for relief of pain.
   G. Trial of sympathetic blocking agents.
   H. Sympathetic lumbar block.
   I. Sympathectomy in selected cases.

IV. *Additional measures in cases with ulcers or superficial gangrene*
   A. Hospitalization at absolute bed rest in a warm room.
   B. Use of an oscillating bed if available.
   C. Warm soakings with normal saline solution.
   D. Local application to infected ulcers or gangrene of sulphonamides or antibiotics in appropriate solution or ointment.
   E. Local application of powdered erythrocytes to clean, healing ulcers.

F Administration of alcohol by mouth b i d or t i d
G Prescription of analgesics as necessary for relief of pain
H Use of sulphonamides or antibiotics orally or parenterally for systemic action, as indicated

V *Additional measures in cases of extensive gangrene, severe ulceration or osteomyelitis*

A Measures as in IV
B Delay in amputation, if possible until demarcation and possible slough
C Amputation at lowest possible level but with due consideration for the future use of a satisfactory prosthesis and only after patient s condition has been made optimal and infection has been controlled
D Amputation at higher level if
1 Pain is excessive or uncontrolled or
2 Gangrene is spreading

VI *Additional measures when case is complicated by an acute arterial occlusion*

A See section on treatment of acute arterial occlusion
B If circulation is reestablished follow measures under III
C If gangrene develops, use measures under IV or V

## THROMBOANGIITIS OBLITERANS
(Buerger s Disease)

Thromboangiitis obliterans is a specific inflammatory and obliterative disease of the arteries and veins It occurs almost exclusively in young men It involves the extremities (and occasionally the viscera as well) and produces ischemia of the tissues and, frequently gangrene Thromboangiitis obliterans involves all three layers of the walls of the vessels This inflammation leads to thrombosis and organization of the thrombus although it is perhaps, recanalized to a minor extent and transforms the occluded vessel into a fibrous cord

### Etiology

The etiology of thromboangiitis obliterans is not known A number of factors are known to influence both the occurrence and the course of the disease

1) *Age* —Thromboangiitis obliterans manifests itself, for the most part, in men between the ages of 21 and 45 The rare cases of thromboangiitis obliterans among children are found in those who smoke early and heavily Cases in which the condition seems first to manifest itself after the 50th year usually prove to be cases of arteriosclerosis obliterans

2) *Sex* —The disease occurs almost exclusively in men The number of reported cases among women are very few but are recently increasing This may indicate either an increase or better recognition of the disease In many of the cases among women, no pathological evidence is submitted to substantiate the diagnosis There is no satisfactory explanation for the rarity of thromboangiitis obliterans among women but there are three theories about it (*a*) that differences in the habits and exposures of the two sexes account for it (*b*) that a sex linked hereditary factor is responsible and (*c*) a biological difference provides women with immunity to the disease

3) *Race* —Thromboangiitis obliterans occurs in all racial groups so far studied It appears to be somewhat more common among Jews than among others but is not as originally thought a disease confined almost exclusively to them

4) *Heredity* —There are only isolated instances of the occurrence of the disease in two or more close relatives

5) *Occupation Trauma Cold* —Repeated studies have failed to show any relationship between the occurrence of thromboangiitis obliterans and occupation even when the occupation is arduous and involves exposure to extreme cold and dampness Trauma is often an aggravating factor and may produce a lesion which by reason of failure to heal normally may first indicate the presence of an extensive obliterative vascular disease Frostbite and fungus infections between the toes may

precipitate the initial open lesion of Buerger's disease

6) *Climate* —Cold weather has a deleterious effect on those with thromboangiitis obliterans; the disease is often first manifested with the onset of winter. Symptoms are aggravated during cold weather, which in controlled cases may cause relapses. This, however, is probably the effect of vasoconstriction superimposed upon the existing arterial insufficiency. Cases of thromboangiitis have been reported from all climates, and removal of patients with the disease from cold to warm climates does no more than relieve vasospasm.

7) *Tobacco* —The smoking of tobacco has a great deal to do with the development of thromboangiitis obliterans and with the unfavorable progression of the disease. The evidence is extensive and definite: (*a*) almost without exception patients with the disease are smokers, most of them heavy smokers. Very few authenticated cases of Buerger's disease among non-smokers have been reported. (*b*) The disease is more severe among heavy than among light smokers. (*c*) The course of the disease is significantly influenced by the patient's use of tobacco. The disease can often be arrested in the early stages solely by abstinence from tobacco. In advanced cases with ulceration or gangrene, the smoking of several cigarettes after a long period of arrest or improvement may cause a sudden dramatic aggravation of the condition. Patients with thromboangiitis who persist in smoking almost invariably do badly. Those who discontinue smoking tend to improve and may exhibit little or no progression of the disease over a period of years. (*d*) Smoking causes vasoconstriction in the peripheral blood vessels of most persons; there is slowing down of the capillary blood flow and a decided drop in the temperature of the skin of the fingertips.

The concept of vascular allergy to tobacco proposed by Harkavy *et al.*, who have reported a high incidence of hypersensitive reactions to skin tests in persons with thromboangiitis, is not widely accepted.

8) *Infection* — The inflammatory character of the vascular lesions has suggested infection by bacteria, viruses or rickettsiae as the cause of the condition.

Dermatophytosis and focal infection have also been suggested as etiologic factors. The evidence for an infectious origin for the disease, though not impressive, is certainly sufficient to encourage further study.

9) *Intravascular Factors* — Hemoconcentration and increased viscosity and increased coagulability of the blood have been reported as precipitating factors in thromboangiitis obliterans. This would lead one to expect intravascular clotting to precede lesions in the walls of the vessels. Actually, though intravascular clotting frequently occurs in Buerger's disease, it is invariably a complication of an already existing inflammatory and obliterative process in the walls of the vessels.

## Pathology

Thromboangiitis obliterans is primarily a disease of the small and medium sized blood vessels of the extremities. It is usually more extensive and more severe in the legs than in the arms. Visceral lesions are rare and usually follow old and extensive peripheral lesions. The disease most commonly involves the anterior tibial, the posterior tibial, and the radial and ulnar arteries; less commonly the plantar, palmar and digital arteries. The small and medium veins are involved less than the arteries. The arterial and venous trunks are involved late in progressive cases, if at all. The arterioles are not affected.

The condition is a distinctly segmental, inflammatory and non-suppurative panarteritis or panphlebitis with associated thrombosis but without necrosis of the vessel wall. Organization of the thrombus occurs vigorously and promptly; recanalization is usually distinctly limited. The lesions in a given case are of different ages, but the involvement of a single segment of a vessel appears to be of a single age. The organic occlusions of the vessels are permanent and essentialy complete. Functionally, the involved vessels are destroyed or hopelessly impaired. There is an extensive development and enlargement of collateral circulation with widespread anas

F Administration of alcohol by mouth b i d or t i d
G Prescription of analgesics, as necessary for relief of pain
H Use of sulphonamides or antibiotics orally or parenterally for systemic action, is indicated

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deal of disagreement about the reported findings and their interpretation

The primary physiological effects of thromboangiitis are impaired blood flow and the resultant ischemia. Impairment of the blood flow may be increased by extensive arteriolar spasm. In cases complicated by thrombophlebitis venous obstruction may contribute to the damage. Changes in the capillaries are not consistent, but atony and dilatation are frequent. These are expressed clinically by intense rubor. Edema is not uncommon. It may result from increased capillary permeability or from increased capillary pressure due to venous stasis and the effects of dependency. Inflammatory reactions may contribute to the edema.

## Clinical Signs

1 *Premonitory Symptoms* — Minor sensory disturbances frequently presage the appearance of the classical symptoms of thromboangiitis obliterans. These include sensations of coldness, burning, formication, tingling, and other types of paresthesias.

2 *Pain* — Pain is ordinarily the presenting symptom and may be one of several types.

*a) Intermittent Claudication* — Claudication is observed in about 75 per cent of the cases and is in general the same as in arteriosclerosis obliterans.

*b) Rest Pain* - Pain at rest, particularly nocturnal pain, is usually described as burning, aching or gnawing and is commonly associated with tenderness. It is often relieved by hanging the affected limb over the side of the bed or by walking about the room. It is often a sign that ulceration or gangrene is imminent.

*c) Pain from Ulcers or Gangrene* — Pain associated with ulceration or gangrene is often severe. It is either continuous or paroxysmal and is often worse at night. Hypesthesia in the area of pain is frequent.

*d) Pain from Inflammation of the Blood Vessels* — Pain from inflammation of the arteries is severe and diffuse. It is often accompanied by signs of localized inflammation. It may produce generalized aching. Pain from the phlebitis which so commonly complicates thromboangiitis obliterans dif-

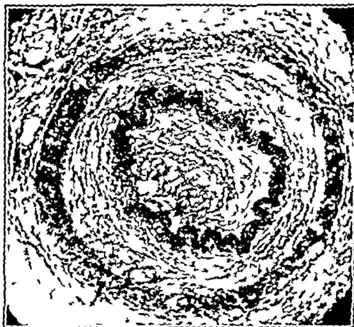


Fig 175 — Thromboangiitis obliterans. The lumen is closed by fibrous tissue which is partially canalized. Hypertrophy of elastica. Elastic tissue stain × 40 (Boyd Textbook of Pathology)

tomoses Ischemia and malnutrition of the tissues are complicated by the effects of trauma and of secondary infection The severity of the disease is in proportion to the speed and extent of the vascular obliteration The outcome in any given case depends largely on the rapidity and completeness with which the active process is suppressed and the collateral circulation is developed

*Gross Changes in the Vessels* —The vessels are contracted the involved segments distinctly indurated The occluding mass in the lumen of the vessel is distinct from the media There may be fresh red thrombus at one or both ends of the older, adherent clot Occlusion of the arteries is the rule that of the veins the exception The extent of occlusion varies, *there may be lengths of* patent lumen between two occlusions Induration usually extends into the adventitia and perivascular tissues and may involve the accompanying vein and nerve as well as the artery

*Histological Changes* —Early changes appear to consist of intimal proliferation focal infiltration of lymphocytes into the intima, and infiltration of lymphocytes and fibroblasts into the adventitia, particularly in the region of the vasa vasorum

In the acute lesions endothelial proliferation is marked and focal intimal infiltration by *lymphocytes usual The lumen is filled* with a thrombus containing endothelial cells and fibroblasts The internal elastic lamina is preserved The medial coat contains fibroblasts and the dilated capillaries in this layer show endothelial proliferation The muscle fibers are usually well preserved There is extensive fibroblastic proliferation in the adventitia, *and the vasa vasorum* are surrounded by foci of lymphocytes The intima of the vasa vasorum proliferates and the medial coat is thickened Leukocytes appear only in small numbers

In old lesions the thrombus becomes increasingly well organized and there is a lack of generalized or extensive canalization The internal elastic lamina is thickened but relatively intact and the *media is not* significantly altered except for infiltrations by fibroblasts and the development of vasa vasorum The earlier fibroblastic reaction in the adventitia is gradually organized *into fibrous connective tissue Fibrosis* characterizes the late lesions and perivascular fibrosis often binds the arteries to vein and nerve The lesions in the veins are similar to those in the arteries

The most striking features of thromboangiitis obliterans are the extensive endothelial proliferation and the dense fibroblastic infiltration The thrombus is a true thrombus although proliferation of the endothelium contributes to the obliteration of the lumen The general architecture of the vessel is discernible in old lesions, despite the intensity of the reaction

*Secondary Pathological Changes* — Ischemia abetted by trauma and infection, produces secondary changes in many tissues *Skeletal structures show the effect of ischemia* there may be atrophy and fibrosis of skeletal muscles osteoporosis of the bones replacement of subcutaneous fat by fibrous tissue and atrophy and distortion of the skin and nails Capillaries, especially those of the digits, may become dilated and atonic

Significant changes in the nerves are common in advanced cases of Buerger s disease There are usually both perineural and perivascular fibrosis and there may be Wallerian degeneration and demyelination Occasionally *the destruction of a nerve may be complete*

Though ulceration and gangrene may occur spontaneously as a result of ischemia these are commonly precipitated by trauma They usually attack the toes but sometimes the fingers the distal half of the foot the entire foot or even the lower leg Ulceration of the foot or leg without involvement of the *toes is almost always due to local trauma* Gangrene is usually dry but may be complicated by secondary infection suppuration or cellulitis with or without lymphangitis

## Pathologic Physiology

The changes in the blood are said to include (1) hemoconcentration (2) alterations of the coagulation factors (3) abnormal concentrations of lipids and (4) altered oxygen content but there is a good

radial and ulnar arteries by means of the Allen test * (4) testing for reflex dilatation by application of heat to the unaffected limbs or to the trunk (Landis and Gibbons) and (5) sympathetic block. Angiography is occasionally necessary.

### Course

Thromboangiitis obliterans tends to be progressive but the rate of progression varies widely. Occasionally a case exhibiting a favorable course is made worse by arteriosclerosis obliterans. Leading students of this disease agree that victims of it who continue to smoke do badly; those who stop smoking may undergo complete and permanent or at least protracted remission.

### Treatment

(Basic principles outlined in section on treatment of arteriosclerosis obliterans)

I. For all patients total and permanent abstinence from the use of tobacco.

II. For patients with claudication only *see* section on treatment of arteriosclerosis obliterans.

III. For patients with claudication and rest pain or ischemic neuritis but without ulceration or gangrene (see section on treatment of arteriosclerosis obliterans).

A. Use warm cradle; heating box not advocated unless under strict thermostatic control.

B. Use nonspecific foreign protein therapy with typhoid H antigen or a typhoid vaccine.

C. If these measures fail to relieve pain consider advisability of sympathetic blocks or a sympathectomy (sympathectomy is method of choice in the presence of marked vasospasm or Raynaud's phenomenon of the digits).

IV. For patients with ulceration, gangrene or infection (*see* section on treatment of arteriosclerosis obliterans) use medical measures to produce vasodilatation; their failure to produce definite improvement indicates need for early sympathectomy.

V. For patients with gangrene, thrombophlebitis or acute arterial occlusion, *see* section on treatment of these conditions.

* *The Allen Test.*—The patient holds his hands in front of him; the examiner presses with his thumbs the radial artery in each of the patient's wrist. The patient then clenches his hands tightly for 10 or 15 seconds and repeats the process until the blood is squeezed out of his hands. With the radial arteries still compressed the patient partially extends his fingers. The return of color to the hands and fingers is then observed. Where the ulnar artery is patent normal color or reactive hyperemia rapidly replaces the pallor. If the ulnar artery is occluded, pallor persists for a variable period. Patency or occlusion of the radial artery may be demonstrated in a similar manner by occluding the ulnar artery and repeating the test.

Grossly impaired pulsations in the arteries of the arms are unusual in arteriosclerosis obliterans. Impairment of these pulsations in either the radial or the ulnar arteries is very common in thromboangiitis obliterans. Unilateral or bilateral obliteration of the ulnar artery as determined by the Allen test strongly favors a presumptive diagnosis of Buerger's disease.

## ACUTE ARTERIAL OCCLUSION

(Arterial Embolism, Acute Arterial Thrombosis)

Sudden occlusion of an artery may result from the development of an intravascular clot *in situ* (thrombosis) or from the lodgement of an unattached and circulating clot arising elsewhere in the vascular system (embolism). It is one of the most dramatic complications of cardiovascular disease but may occur as the result of a trauma or of a disturbance in the coagulation mechanism of the blood. Occlusion of small and relatively minor vessels may not be serious; occlusion of a major artery may produce gangrene. The differential diagnosis between thrombosis and embolism is often difficult or impossible without exploration of the involved vessel but the distinction is important for emboli most often arise in the heart from mural thrombi which not uncommonly release additional emboli.

### Etiology

The heart is the chief source of systemic arterial emboli. These are usually detached

fers in no essential from that of thrombophlebitis from any cause

*e) Pain from Sudden Arterial Occlusion* — Sudden arterial occlusion produces severe pain that radiates down the limb and is often associated with muscular cramps. The limb peripheral to the occlusion becomes cold, clammy, numb, and either pale or cyanotic. The pulses distal to the occlusion are not palpable. The pain tends to subside in from 24 to 72 hours but may recur upon movement or manipulation of the limb. This pain is undoubtedly due to ischemia resulting from organic occlusion and the associated vasospasm. When the collateral circulation has become adequate and the vasospasm is relieved, this pain disappears. Residual paresthesias, numbness, and tingling, and paroxysms of pain and claudication tend to persist for a long time.

*f) Pain from Ischemic Neuritis* —When the nerves accompanying the involved arteries are damaged by ischemia and the periarterial spread of the inflammatory process, there is often a sharp lancinating pain that radiates peripherally. This pain is often both paroxysmal and diffuse. Section of the involved nerve may be necessary for relief. The pain tends to occur late in the course of the primary disease.

3. *Temperature Changes* —A sensation of coldness may occur in the distal portion of a limb, especially if the limb is exposed to temperatures below room temperature. This coldness may alternate with a feeling of burning that occurs when the limb is warmed.

4. *Color Changes* —The striking rubor with or without cyanosis which appears on dependency in a limb afflicted with occlusive arterial disease is due to compensatory dilatation of the minute vessels which contain blood highly saturated with oxygen. Cyanosis appears as the relatively stagnant blood slowly loses its oxygen to the tissues. Upon elevation of the limb, the rubor yields to pallor as the blood drains out and fresh blood is unable to flow in freely.

In a normal person lying supine, the normal color of the foot is maintained on elevation to 180° and only slight rubor occurs on dependency to 60° or less. Abnormal pallor on elevation can be hastened and accentuated by massaging the foot toward the body and by having the patient move his toes actively. Rubor and pallor usually appear in a patchy manner due to differences in the speed with which the vessels fill and empty. These color changes, even when the pedal pulses are palpable, constitute evidence of arterial insufficiency.

5. *Edema* —Edema commonly occurs in Buerger's disease as a result of (1) obstruction by phlebitis of the venous return, (2) increased intracapillary pressure due to inactivity and dependency, or (3) inflammation.

6. *Phlebitis* —Superficial or deep phlebitis occurs in about half the cases of thromboangiitis obliterans. It may be the initial sign of the disease. Thromboangiitis should always be thought of when phlebitis occurs without clear cause in young or middle aged men, especially if it recurs in the legs or feet.

7. *Trophic Changes* —As a result of impaired blood supply, the skin becomes tense, shiny, dry, scaly, and often pigmented. The nails become thickened, ridged, and discolored and fail to grow.

Ulcers and fissures develop upon the slightest trauma and infection supervenes readily. Fungus infections between the toes produce deep fissures. The ulcers and fissures in thromboangiitis are characteristically deep, sharply demarcated, moist, purulent, inflamed and excruciatingly tender.

8. *Gangrene* —The ulcers and fissures tend to progress to frank gangrene involving the digits or portions of the hand or foot. Occlusion of major vascular channels leads to more or less massive gangrene which is often moist and necrotic. The pain of the gangrene in Buerger's disease is excruciating.

*Differential Diagnosis* — See table p. 1100

## Diagnostic Procedures

Since thromboangiitis obliterans is essentially a systemic vascular disease, the physical examination must be painstaking and should include (1) systematic palpation of the peripheral arteries, (2) oscillometry, (3) determination of the patency of the

radial and ulnar arteries by means of the Allen test,* (4) testing for reflex dilatation by application of heat to the unaffected limbs or to the trunk (Landis and Gibbons) and (5) sympathetic block. Angiography is occasionally necessary.

### Course

Thromboangiitis obliterans tends to be progressive, but the rate of progression varies widely. Occasionally a case exhibiting a favorable course is made worse by arteriosclerosis obliterans. Leading students of this disease agree that victims of it who continue to smoke do badly; those who stop smoking may undergo complete and permanent or at least protracted remission.

### Treatment

(Basic principles outlined in section on treatment of arteriosclerosis obliterans)

I. For all patients: total and permanent abstinence from the use of tobacco.

II. For patients with claudication only: *see* section on treatment of arteriosclerosis obliterans.

III. For patients with claudication and rest pain or ischemic neuritis but without ulceration or gangrene (see section on treatment of arteriosclerosis obliterans):

A. Use warm cradle; heating box not advocated unless under strict thermostatic control.

B. Use nonspecific foreign protein therapy with typhoid H antigen or a typhoid vaccine.

C. If these measures fail to relieve pain, consider advisability of sympathetic blocks or a sympathectomy (sympathectomy is method of choice in the presence of marked vasospasm or Raynaud's phenomenon of the digits).

IV. For patients with ulceration, gangrene or infection (*see* section on treatment of arteriosclerosis obliterans), use medical measures to produce vasodilatation; their failure to produce definite improvement indicates need for early sympathectomy.

V. For patients with gangrene, thrombophlebitis or acute arterial occlusion, *see* section on treatment of *these conditions*.

*The Allen Test.*—The patient holds his hands in front of him; the examiner presses with his thumbs the radial artery in each of the patient's wrist. The patient then clenches his hands tightly for 10 or 15 seconds and repeats the *process until the blood is* squeezed out of his hands. With the radial arteries still compressed, the patient partially extends his fingers. The return of color to the hands and fingers is then observed. Where the ulnar artery is patent, normal color or reactive hyperemia rapidly replaces the pallor. *If the ulnar artery is occluded, pallor* persists for a variable period. Patency or occlusion of the radial artery may be demonstrated in a similar manner by occluding the ulnar artery and repeating the test.

Grossly impaired pulsations in the arteries of the arms are *unusual* in arteriosclerosis obliterans. Impairment of these pulsations in either the radial or the ulnar arteries is very common in thromboangiitis obliterans. Unilateral or bilateral obliteration of the ulnar artery as determined by the Allen test strongly favors a presumptive diagnosis of Buerger's disease.

## ACUTE ARTERIAL OCCLUSION

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### Etiology

The heart is the chief source of systemic arterial emboli. *These are usually detached*

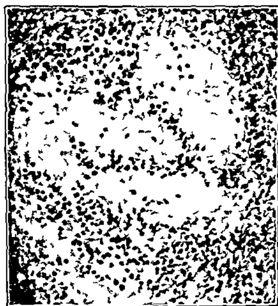


FIG 176 —Fresh pale thrombus on ventricular endocardium composed of leukocytes and platelets (pale areas) Photomicrographs (Bell Textbook of Pathology )

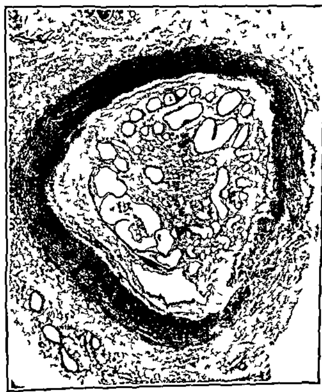


FIG 177 —An arterial thrombus showing canalization Photomicrograph (Bell Textbook of Pathology )

portions of intracardiac mural thrombi occurring in rheumatic heart disease with auricular fibrillation, myocardial infarction with mural thrombosis, acute or subacute bacterial endocarditis involving the mitral or aortic valves, and congestive heart failure. Emboli may arise in the arteries themselves from thrombi associated with aneurysms, arteriosclerotic plaques, trauma or inflammation. Occasionally paradoxical emboli arise in the systemic veins and pass into the systemic arteries through a patent foramen ovale when the pressure in the right auricle is increased.

Localized thrombosis in an artery may result from an inflammatory disease such as thromboangiitis obliterans, periarteritis nodosa or mycotic arteritis; from the degenerative disease arteriosclerosis obliterans; from trauma such as gunshot and stab wounds or severe extrinsic trauma; or from pressure as that exerted by a cervical rib. Thrombosis occurs with unusual frequency in connection with certain infectious diseases (*e.g.*, typhoid fever, pneumonia, *etc.*) with blood dyscrasias (especially polycythemia) and with heart disease producing congestive heart failure. It is also an important sequel to extensive surgical procedures. Sudden and severe multiple arterial occlusions associated with an increased coagulability of the blood and an increased platelet count have been described as *idiopathic thrombophilia*.

## Pathology

Except under experimental conditions it is unlikely that thrombosis is ever the result of a single factor.

In general, three important mechanisms predispose to thrombosis: disturbances in the integrity of the endothelial lining of the vascular tree, as by inflammation or trauma; disturbances in the blood flow, systemically, as in congestive heart failure, or locally, as by extrinsic pressure or intrinsic disease (*e.g.*, arteriosclerosis); and alterations in the coagulability of the blood. Hypercoagulability of the blood may be systemic, as when hyperprothrombinemia exists, or local, as when the output of thromboplastin is increased by local tissue damage.*

## Clinical Signs

Pain in acute arterial occlusion may occur abruptly and be excruciating. But it may occur gradually and not be severe at all. Numbness, coldness and tingling occur in various combinations, however, with or without pain. Occasionally there is loss of muscular power.

The affected limb soon becomes pale and either remains so, assuming a patchy cyanotic pallor, or regains its color only gradually. This depends on the efficiency of the collateral circulation and the relief of the associated vasospasm. The pulse is often lost for a considerable distance proximal to the actual occlusion; this is due presumably to vasospasm, for the pulse returns as vasospasm is relieved.

The chief clinical findings are (1) lowered surface temperature distal to the occlusion, (2) collapsed superficial veins, (3) pallor, (4) diminished reflexes, (5) impaired sensation, (6) loss of muscular strength, and, most important, (7) sudden absence of arterial pulsations previously present.

Systemic manifestations vary widely and in the main depend on the general condition of the patient and the nature of coëxisting disease. In many cases the symptoms of the primary disease overshadow the manifestations of the occlusion; in others the patient becomes suddenly worse as the result of acute occlusion and may go into actual shock.

## Course

The duration of the symptoms that follow an acute occlusion also varies widely; it chiefly depends on the effectiveness of the collateral circulation and the relief of vasospasm. If marked vasodilatation occurs or

* Polycythemia vera, a hematogenous disease, is often associated with peripheral vascular diseases. Thrombophlebitis and sudden arterial occlusion by thrombosis are common complications of polycythemia. Patients with polycythemia usually die of intravascular thrombosis. Occasionally thromboangiitis obliterans is associated with polycythemia.

can be induced, the symptoms may be relieved in a matter of a few hours Symptoms *ordinarily subside* spontaneously in from 24 to 72 hours but either recovery or gangrene may follow In many cases the symptoms of acute occlusion merge into those of ischemic neuritis, the severe paroxysmal pain of which may persist for weeks or months Even when recovery occurs without gangrene or ischemic neuritis, certain stigmata of impaired arterial circulation—vasomotor changes, coldness, intermittent claudication and hyperesthesia—are likely to remain

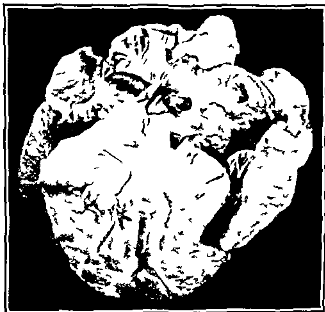


Fig 178 —Paradoxical embolism Heart showing an embolus which was passing from the right auricle through a patent foramen ovale (Bell Textbook of Pathology )

## Prognosis

The prognosis in acute arterial occlusion depends on (1) the artery involved and the level at which it is involved (2) the kind of occlusion—*i e* whether it is due to thrombosis or emoblism (3) the degree of associated vasospasm and the speed with which it is relieved, (4) the efficiency of the collateral circulation, once vasospasm is relieved, (5) the age and general physical condition of the patient (6) the nature of the primary disease and its influence on the general condition of the patient his vascular tree, and his local tissues (7) the promptness and efficiency of treatment

If only the simplest conservative treatment is applied to acute arterial occlusions of major arteries in the extremities, about half the cases will develop gangrene Diagnosis and treatment must be prompt

Age *is an important consideration for* older patients are usually in poorer general condition than younger ones and develop collateral circulation less readily besides they usually exhibit circulatory impairment as a result of atheromatous changes Gangrene occurs in more than three quarters of the patients over 60 but only in slightly more than a third of those under 60

When arterial thrombi occur in patients suffering from severe infections or congestive heart failure the prognosis is generally poor for the intravascular clotting usually indicates failing circulation In these cases peripheral *thromboses are often followed by* pulmonary embolism cerebral vascular occlusion or coronary thrombosis When simple thrombosis occurs after trauma or an operation the prognosis is relatively good

TREATMENT

The immediate treatment is as follows

1) The patient is put to bed in a hospital room maintained at a temperature of from 80 to 85° F

2) If available an oscillating bed is used Otherwise the head of the hospital bed is elevated on blocks 6 inches high

3) The patient's foot and leg are wrapped loosely in cotton batting but neither heat above 90° F (32 2° C) nor refrigeration are applied directly to the involved extremity (Refrigeration may be used as preamputation anesthesia)

4) Reflex heat is applied to the abdomen or to the lumbosacral area by means of a heating pad

5) Morphine or a morphine substitute is given parenterally to relieve pain Relief of vasospasm (*see* below) may so improve the circulation as to make opiates unnecessary after the *initial* period of treatment

6) Vasospasm is relieved and maximum vasodilatation obtained as follows

*a*) Whiskey or brandy is given (1 or 2 ounces) every 3 to 6 hours depending on the tolerance of the patient

*b*) Papaverine hydrochloride 0 5 to 1 0 grain (0 03—0 06 gram) is given intravenously or intra-arterially proximal to the occlusion The injection of 1 grain of papaverine directly into the brachial or femoral arteries will frequently produce a striking increase in warmth and occasionally a conspicuous flush in extremities which have previously been cold and cyanotic Such a response may occur in limbs which have not responded to a sympathetic block The injection may be repeated every 4 to 6 hours if the response is good but not so often as to produce drowsiness or disorientation The intra-arterial injection must be made cautiously

*c*) Paravertebral sympathetic block is performed This may produce satisfactory peripheral vasodilatation but must be repeated several times within the first 2 or 3 days to maintain the effect

*d*) Sympathetic blocking agents are used (either tetraethylammonium chloride [Etamon®] in doses of from 3 to 10 cc intramuscularly every 3 to 6 hours or *Priscoline®* in doses of from 50 to 100 mg parenterally at similar intervals)

Sympathectomy is performed if severe vasospasm persists despite more conservative measures The results of sympathectomy cannot be predicted from the effects of the sympathetic blocking agents or of paravertebral blocks

7) Anticoagulants are used to prevent propagation of the intravascular clot and further thromboembolic phenomena To produce a prompt anticoagulant effect heparin should be administered immediately and Dicumarol® also if the patient is to be maintained on the latter drug The anticoagulant therapy may be delayed or interrupted briefly if surgery is performed immediately

8) The cause of the acute arterial occlusion (as also the source of the embolus in instances of embolism) is ascertained If this is found to be an intracardiac mural thrombus as in cases of rheumatic heart disease with auricular fibrillation further thromboembolic episodes may be anticipated unless long term anticoagulant therapy is used

9) Embolectomy is done if a massive embolus occurs in a major arterial trunk or bifurcation (as in the aortic bifurcation where the result is total blocking of the iliac arteries and paralysis and coldness of the legs) If done at all the operation should be done from 4 to 10 hours after the occurrence of the embolus Anticoagulant therapy should be used postoperatively

In favorable cases the patient is kept in bed in a warm environment until the circulation has become adequate An oscillating bed if available is used for eight hours a day or more Alcohol sedatives analgesics and sympathetic blocking agents may be continued until the circulation is reestablished

If gangrene develops the infection should be controlled by the use of antibiotics locally and systemically Amputation if necessary should be performed at the optimum time

## OTHER DISEASES OF THE ARTERIES

### Aneurysms

An aneurysm, the abnormal dilatation of a blood vessel, results from localized weakness in and consequent stretching of the vessel's wall. The term is restricted to arterial aneurysms, most venous dilatations are called *varicosities*. The term *aneurysm* should not be applied to arteriovenous fistulas, in combination with which aneurysms not uncommonly occur.

Table 52.—Etiological Classification of Aneurysms

*A* Arteriosclerosis
*B* Syphilis
*C* Other infections (Mycotic aneurysm) *e g* tuberculosis actinomycosis septicemia subacute bacterial endocarditis typhoid fever *etc*
*D* Congenital weakness of the arterial wall *e g* in the anterior portion of the Circle of Willis and its branches
*E* Trauma producing either true or false aneurysms with or without arteriovenous fistulas
*F* Periarteritis nodosa and other necrotizing arteritides usually producing small aneurysms

Table 53.—Pathological Classification of Aneurysms

| | |
|---|---|
| Fusiform aneurysm | A rather uniform spindle shaped or fusiform dilatation of a segment of an artery |
| Saccular aneurysm | A definite sacculation or outpouching from an artery results from a highly localized weakness of the media |
| Dissecting aneurysm | Rupture of the inner layers of the wall of an artery permits the blood to dissect for varying distances between the inner and outer layers of the wall. At the distal end of the dissection communication with the lumen may be re-established or rupture may occur into the surrounding tissues or body cavity |
| False aneurysm | Complete rupture of all coats of the artery, occurs with the formation of a sac the walls of which are composed of successive layers of blood clot. Especially common in the popliteal space |

### Pathology

*Arteriosclerotic Aneurysms.*—An arteriosclerotic aneurysm usually forms when the medial coat of an artery undergoes focal destruction and the muscle fibers are replaced by fibrous tissue. This may occur in any artery. In the early stages all arteriosclerotic aneurysms are fusiform or saccular. There is a tendency for dissection to follow, and, not infrequently, false aneurysms are formed. Saccular aneurysms are most commonly found in the abdominal aorta and popliteal arteries. Fusiform aneurysms are most common in the thoracic and abdominal portions of the aorta. Dissecting aneurysms are generally confined to the aorta, of which they may involve any portion, and even involve its branches. Arteriosclerotic aneurysms usually occur in persons over 50 and are most common in men. Complete rupture is uncommon but thrombosis is a frequent complication.

*Syphilitic Aneurysms.*—The aneurysms of tertiary syphilis are confined almost exclusively to the aorta and are most frequently found in the ascending portion and the arch. Sometimes, however, they involve the abdominal aorta and occasionally the peripheral vessels. These aneurysms probably result from inflammatory lesions involving the vasa vasorum, impaired nutrition of the media results in focal degenerative changes. Leutic aneurysms are fusiform or saccular, they may enlarge rapidly or very slowly (over a period of years). Some become enormous and eventually erode through resistant structures. Death not uncommonly follows rupture of such an aneurysm, massive hemorrhage occurs into one of the body's cavities or tracts.

*Mycotic Aneurysms.*—These occur in arteries involved in suppurative processes which weaken the media to the point of dilatation or rupture. Local abscesses are a common site of aneurysm formation. A mycotic aneurysm tends to occur where the artery is relatively unsupported by skeletal

TABLE 54 — CHARACTERISTICS OF ANEURYSMS ACCORDING TO THEIR COMMON SITES

| *Type and Location of Aneurysm* | *Common Etiologies* | *Average Age of Appearance* | *Sex Preponderance* | *Prognosis* |
|---|---|---|---|---|
| AORTA | | | | |
| Dissecting Aneurysm | Arteriosclerosis usually syphilis uncommonly Hypertension present in 50 60 % of cases | 60 years | Males 6 1 | Sudden death 33% Death within 24 hours 50% Survival for 1 month 10% |
| Saccular and Fusiform Aneurysm Thoracic Aorta | Syphilis in the majority of cases less commonly arteriosclerosis rarely trauma | 60 years | Men 4 1 | Av length of life without antiluetic therapy 1-2 years with treatment 5 years or more |
| Saccular and Fusiform Aneurysm Abdominal Aorta | Majority due to arteriosclerosis 5-10% due to syphilis other causes rarely | 60 years | Males 2 1 | Prognosis somewhat better than for thoracic aneurysm |
| INTRA ABDOMINAL ARTERIES OTHER THAN THE AORTA | Most common causes are mycotic or necrotizing arteritis or periarteritis nodosa | Any age | No significant sex variation | Prognosis is largely dependent on underlying disease |
| LARGE ARTERIES LOWER EXTREMITIES | Most common cause is arteriosclerosis in younger persons arteritis and trauma | Any age | No significant sex variation | Prognosis is relatively good Ligation and obliteration usually possible |
| LARGE ARTERIES UPPER EXTREMITIES OR NECK | Trauma commonly arteritis or arteriosclerosis uncommonly | Any age | No significant sex variation | Prognosis relatively good Ligation and obliteration often possible |
| SMALL PERIPHERAL ARTERIES | Usually due to periarteritis nodosa | Any age | No significant sex variation | Prognosis is that of underlying disease Lesion usually can be excised for diagnosis |



FIG 179 — Aneurysm of the aorta (Boyd Pathology of Internal Diseases)

muscle and is subject to frequent bending, as in the *popliteal, femoral, axillary*, and brachial arteries and in Scarpa's triangle

*Aneurysms Due to Periarteritis and Necrotizing Arteritis.*—Local muscular necrosis in small and medium-sized arteries results in small aneurysms that give the vessels a nodular or beaded appearance. The nodular lesions of temporal arteritis are often tiny aneurysms. Localized intimal proliferation and localized periarteritis occur here. The aneurysms may be true or false and may develop progressively in widely distributed arteries. There is no evidence of bacterial infection in these cases.

*Congenital Aneurysms.*—When a congenital aneurysm exists, the medial coat is absent or thin and underdeveloped in segments of an artery. Congenital aneurysms are rather common in the Circle of Willis and its branches and in the intracranial portion of the internal carotid arteries. Rupture of such an aneurysm is one of the common causes of fatal cerebral hemorrhage. Congenital aneurysms may be multiple. In one case observed, they were present in both popliteal arteries, both axillary arteries and the aorta. They may also be found in association with hemangiomas and with congenital arteriovenous fistulas.

*Traumatic Aneurysms.*—True or false aneurysms, more commonly the latter, may be caused by penetrating wounds. Even when there is only slight external bleeding a hematoma may form and develop into a false aneurysm.

## DISSECTING ANEURYSM

### Clinical Signs

The onset is sudden and often associated with physical exertion or emotional strain. The pain is usually excruciating and is commonly precordial so that it may be ascribed to acute coronary occlusion. The pain however may originate between the scapulae, in the abdomen or in the lumbar region. It tends to spread from front to back or vice versa, and then down into the abdomen or the legs. It may radiate to the neck, sometimes (though seldom) to the arms. The pain may persist for days. Occasionally, the attack is painless and manifested by acute cardiac failure due to aortic reflux. Shock, collapse and severe vomiting are usual. Further signs depend on (1) the degree of pressure on adjacent structures and (2) the degree of interference with the blood flow through the branches of the aorta.

Pressure on the great veins may produce venous engorgement and cyanosis. This may be asymmetrical, so that the venous pressure is different for each arm. Pressure on the recurrent laryngeal nerve may cause aphonia, on the esophagus, dysphagia, and on the lung, dyspnea, collapse of the lower lobe and pleural effusion.

Involvement of the orifices of the innominate or the subclavian arteries may alter the radial pulse. Involvement of the carotid arteries may produce syncope and hemiplegia. Involvement of the renal arteries may result in hematuria, or anuria. Loss of normal arterial pulsation in the extremities may in combination with the above signs suggest the diagnosis. The limbs may become pale, cold, cyanotic and numb. Frequently there is loss of motor function and the reflexes are depressed or suspended.

Dissection into the pericardial sac or the pleural cavity usually causes immediate death. The orifices of a coronary artery may be involved; this leads to coronary occlusion with myocardial infarction. Involvement of the root of the aorta renders the valves incompetent and new murmurs appear. The left ventricle dilates acutely and intractable heart failure may supervene.

### Course

Many patients die at once, but some survive. Recovery may even be sufficiently complete to permit a life of reasonable activity for months or years.

### Diagnosis

An onset of precordial pain may suggest coronary occlusion. The diagnosis of dissecting aneurysm is practically certain if three cardinal groups of signs appear:

1) loss of circulation and motor function in the legs

2) evidence of pressure on contiguous structures and
3) previously absent aortic murmurs

### Laboratory Findings

The roentgen examination of the chest will frequently disclose an irregular shadow of variable density on the left side. Pulsations may or may not be evident or may change from time to time. An electrocardiogram may rule out coronary occlusion with myocardial infarction unless this has occurred as a complication. There may be some degree of leukocytosis and of anemia. The urine may show hematuria if the renal arteries are involved, or there may be anuria.



Fig 180.—Dissecting aneurysm of abdominal aorta. The media is split into two layers by a mass of blood. ×15. (Boyd, Pathology of Internal Diseases.)

## NON-DISSECTING ANEURYSM

Common sites of arteriosclerotic aneurysms are the aorta and the popliteal, innominate, subclavian and common carotid arteries.

Symptoms of non-dissecting aneurysm of the aorta vary widely, depending on the etiology, size, shape and location of the aneurysm. Though aneurysms may be painless until they reach considerable size, pain due to pressure and traction on surrounding structures is a common symptom. It is often substernal and may be transmitted to the neck, shoulders, arms or back. It may be severe. Large aneurysms may obstruct the vena cava. There may also be symptoms as a result of tracheal or bronchial obstruction, among them dyspnea and a brassy cough. Pressure on the recurrent laryngeal nerve may produce hoarseness. There may be numbness in the arms. A systolic murmur with or without a diastolic component is commonly heard over the aortic area. There may be widening of the upper mediastinum on percussion.

Abdominal aneurysms are symptomless in about half of the cases. They may be painful, however, the pain being felt in the abdomen or lower back. Numbness or weakness of the legs may occur. The aneurysm can frequently be palpated as a pulsating mass. A systolic bruit is present in a few cases. Aneurysms of intra-abdominal vessels other than the aorta are not often diagnosed during life except at the time of laparotomy. However, the routine use of the stethescope over areas other than the heart and lungs has resulted in discovery of intra-abdominal aneurysms.

Aneurysms of the arteries of the arms and legs usually produce no acute symptoms unless *rupture occurs*. *Pain occurs upon* rupture, during periods of rapid enlargement, or as a result of pressure on a nerve. This last may cause paresthesias or paralysis. Pressure on a vein may produce venous obstruction and insufficiency. Sudden arterial occlusion as a result of thrombosis or embolism commonly occurs in the aneurysm or distal to it. The diagnosis is usually not *difficult if the* aneurysmal dilatation is palpable. An expanding pulsation in a vessel definitely wider than normal is pathognomonic. A systolic bruit can sometimes be heard.

### Laboratory Findings

Roentgen examination is the most valuable *procedure in diagnosing* an aneurysm and in delineating its size, shape, and location. Pulsations are often visible in aneurysm of the thoracic aorta but owing to thickening of the wall by blood clot may not be. In the absence of pulsations, a typical location, size, and shape are often sufficient identification. X rays are also of value in abdominal aneurysm. The characteristic picture is that of a tumor *in* the region of the aorta, a tumor with a thin line of calcium in its wall. In questionable cases, *contrast angiography of the aorta (aortography)* can be performed. Radiological examination of arteriosclerotic aneurysms in peripheral vessels is diagnostic when the expanded arterial wall is delineated by a thin line of calcification. Angiography is most useful in localizing and delineating aneurysms of peripheral arteries.

### Treatment

There *is no* medical treatment for aneurysms *per se*. Symptomatic and palliative measures are indicated. In a case of luetic aneurysm, however, the syphilis should be treated conservatively with an initial course of bismuth followed by *carefully graded* doses of arsphenamine. When fully evaluated penicillin may be the therapeutic agent of choice. Surgical measures developed for the extirpation or eradication of aneurysms in various locations are frequently indicated but are beyond the scope of this discussion.

## ARTERIOVENOUS FISTULAS

An arteriovenous fistula is an abnormal *communication* between *an artery* and a vein. It may be either congenital or acquired; if the latter, it is most commonly the result of a gunshot wound, a knife wound, or a flying projectile wound.

### Congenital Arteriovenous Fistula

*Etiology*.—Congenital arteriovenous fistulas arise from the failure of the common embryological anlage to differentiate into artery and vein.

*Pathology*.—Arteriovenous fistulas, whether congenital or acquired, may occur anywhere *in the body*. *Each anastomosis may have* one or more of the following characteristics: (1) a direct communication between an artery and a vein, (2) an aneurysmal sac between an artery and a vein, (3) an aneurysmal sac on the arterial side with a communication to the vein, (4) a common opening from an artery and a vein into an aneurysmal sac. In the congenital type, there may be large pools or sinuses with which surrounding arteries communicate through multiple channels. These venous *sinuses or tracts eventually empty* into definite veins.

### Sites

Most demonstrable congenital fistulas occur in the extremities, but they may occur elsewhere. They are apt to be multiple when in the extremities. All types of organs and tissues may be involved, including the viscera and the bones. Similarly, all regions of the body, including the cranium and its content, may be the site of fistulas.

### Clinical Signs

(1) Varicose veins are almost always present in association with congenital arteriovenous fistula, and their occurrence at an early age should always suggest this diagnosis. (2) Ulceration or gangrene may

occur (3) A port wine nevus (birthmark) often indicates congenital arteriovenous fistula When on one of the extremities such a birthmark should especially suggest such a communication (4) There is usually an exaggerated growth of hair and increased sweating in regions affected by congenital fistula (5) An increased length of the limb is also usual (6) The temperature of the skin of the affected member is usually higher than that of the contralateral normal extremity (7) Compression of the artery above the site of a fistula usually slows the heart rate by from 5 to 50 beats a minute (8) The oxygen content of the venous blood in the vein proximal to the fistula is increased (this is demonstrated by its bright red color and high degree of oxygen saturation) (9) The lesion may frequently be demonstrated conclusively by arteriography

## ACQUIRED ARTERIOVENOUS FISTULA

### Clinical Signs

*Immediate Manifestations* —A wound which produces the fistula usually bleeds profusely A thrill and bruit continuous through the cardiac cycle appear immediately or after some hours or days

*Delayed Manifestations* —(1) Relative venous insufficiency may be manifested by the appearance of varices edema stasis pigmentation chronic indurative cellulitis and ulceration The ulceration of arteriovenous fistula may affect the distal part of the foot an unusual location for ulceration from ordinary chronic venous insufficiency (2) Gangrene of the digits or the area distal to the shunt may occur as a result of ischemia (3) A disproportionate increase in the length of the limb may occur in cases in which the fistula is acquired before the epiphyses close (4) Thrill and bruit continuous through the cardiac cycle accentuated during systole and of a coarse machine-like quality are pathognomonic (5) The temperature of the skin of the extremity distal to the fistula is usually warmer than that of the normal limb at corresponding levels This is invariably true in the neighborhood of the fistula and commonly so of the toes (6) There may be cardiac enlargement though this is often not marked If the fistula is large cardiac failure may occur

### Diagnosis

Suspect traumatic arteriovenous fistula whenever (1) varicose veins are marked unilateral or not otherwise readily explicable (2) chronic venous insufficiency appears after an injury (3) one limb is warmer and or longer than its companion (4) the patient is aware of a murmur in the region of a penetrating wound The presence of the typical continuous thrill and bruit is diagnostic and confirmatory findings include those already enumerated

### Laboratory Findings

The following laboratory findings are valuable (1) increased oxygen saturation of the venous blood in the region of or proximal to the fistula (2) increased venous pressure in the veins leading from the shunt (3) increased cardiac output (4) increased blood volume (5) increased oscillometric readings distal to the shunt in most instances (6) characteristic arteriographic findings which will demonstrate the site of the lesion its extent and perhaps the mechanism of the circulation below the shunt

### Treatment

When arteriovenous fistulas are single or few in number they can be excised successfully But the problem is often complicated by the fact that the communications are numerous Ligation of the artery proximal to the site of multiple communications or simultaneous ligation of the artery and the vein are of little value When a single digit is involved amputation is advisable Treatment with radium is useful when the radium can be applied to superficial angiomatous regions over the dilated vessels Occasionally injection of the superficial vein with sclerosing solutions such as those used in the treatment of varicose veins may be of value A simple yet sometimes satis

factory method of treatment, particularly when the fistulas are in the legs or feet, is that of compressing the abnormal connections by rubber or elastic bandages

The treatment in most cases is surgical

## COARCTATION OF THE AORTA

Coarctation of the aorta is a localized narrowing of the aorta, usually in the vicinity of the insertion of the ductus arteriosus, which sometimes remains patent There are two chief types of coarctation the infantile and the adult, although all degrees of gradation occur between these

### Etiology

Coarctation of the aorta is a congenital anomaly or developmental defect The infantile type which is uncommon consists of a narrowing of the entire isthmus that part of the aorta between the left subclavian artery and the ductus arteriosus and sometimes of the proximal portion of the arch as well During fetal life the isthmus remains hypoplastic since blood enters the descending aorta largely through the ductus arteriosus This fetal condition may persist for a few weeks or months after birth but it rarely persists until adult life In the infantile type of coarctation the hypoplasia of the isthmus persists and the isthmus may be no more or little more than a fibrous cord

The adult type of coarctation consists of a very localized constriction of the aorta at or near the insertion of the ductus arteriosus It is much more common than the infantile type The ductus arteriosus may remain patent or there may be other associated cardiovascular anomalies All grades of narrowing occur from slight to complete obliteration of the lumen

### Incidence

Coarctation of the aorta one of the half dozen more common congenital anomalies was present in 142 of the 1000 cases of congenital cardiovascular defects reported by Abbott In her series 37 cases were of the infantile type and 105 cases of the adult type The defect has been noted more frequently in the male than in the female

### Pathological Physiology

The proximal part of the aorta may be hypoplastic, or dilated and is often involved in atheromatous degeneration The aortic valves are commonly bicuspid and may become calcified The blood pressure in the arms is usually elevated but as a result of anomalies in the great vessels, may be different in each arm Usually hypertrophy of the left ventricle eventually occurs The smaller arteries and arterioles of the arms are normal

The cause of the hypertension of the upper part of the body is thought to be due to a decrease in the renal blood flow Since glomerular filtration is normal the interference is thought to be in the glomerular efferent arterioles and to be rather like an arteriospasm The cardiac output is increased in most cases but may be normal unless heart failure supervenes The peripheral blood flow is high

The systolic blood pressure is reduced distal to the coarctation and in the legs but the diastolic pressure may remain normal The pulse in the legs is usually weak and retarded In some cases neither the blood pressure nor the pulses in the legs can be obtained by clinical methods

The collateral circulation consists of anastomoses between the aorta and the following arterial systems scapular cervical internal mammary intercostal and spinal When the ductus arteriosus is patent a collateral circulation may not develop

*Symptoms* —In the adult type of coarctation there may be neither symptoms nor signs Symptoms may develop only after years and then be referable to the hypertension, to cardiac failure or to other complications

### Signs

In highly developed coarctation there are a number of important physical signs (1) inequality in blood pressure and pulse between the arms and the legs (the brachial

systolic pressure is ordinarily much elevated, the femoral systolic pressure low, and the femoral pulse small); (2) evidence of collateral circulation between the upper and lower parts of the body, the vessels being dilated and tortuous and sometimes exhibiting palpable or visible pulsations; (3) prolonged systolic murmurs, often accompanied by thrills, felt over the precordium and back and often along the dilated tortuous anastomotic vessels; (4) enlargement of the heart and sometimes heart failure due to associated cardiac lesions and to the hypertension itself.

### Course and Complications

The course of patients with coarctation varies tremendously, depending on the degree of the narrowing of the aorta, the associated cardiovascular anomalies, and the occurrence of complications. The death of such patients early in life usually occurs as a result of congestive heart failure, rupture of the aorta, cerebrovascular accident, or bacterial endarteritis.

### Laboratory Findings

The roentgen examination of the chest, utilizing the oblique as well as the anteroposterior position, is invaluable in demonstrating the presence and characteristics of coarctation. There is a decrease in the size of, or an absence of, the aortic knob, frequent evidence of dilatation of the ascending aorta, and in advanced cases notching of the ribs. Of critical value is the use of retrograde aortography.

### Diagnosis

The diagnosis of coarctation should be considered in all instances of unexplained hypertension. It is to be suspected particularly when hypertension occurs in childhood or youth. In advanced cases the differences in blood pressure and pulse between the arms and legs, the prolonged systolic murmur widely transmitted down the back and often accompanied by thrill, and the evidence of collateral circulation make the diagnosis relatively simple.

### Treatment

Many cases of coarctation can now be corrected surgically by excision of the constricted area and anastomosis of the aorta or by insertion of an arterial graft.

### Prognosis

Patients with coarctation may live to an advanced age but are always liable to sudden death from rupture of the aorta or of the commonly associated congenital aneurysm of the cerebral circulation, from serious illness, or from cardiac failure or endarteritis. The average life span of persons with untreated coarctation is about 30 years. The surgical treatment seems to offer hope of an increased life span, but longer periods of observation are essential for final conclusions.

## DISEASES OF THE VEINS

The organic diseases of the veins may be divided into the obstructive and the nonobstructive. The first include those due to intrinsic occlusion, as in venous thrombosis and in neoplastic invasion of a vessel, and those due to extrinsic pressure, as from a gravid uterus, a growing malignant tumor, or the wearing of constricting garments. By far the most common lesions of this type are the two forms of venous thrombosis, thrombophlebitis and phlebothrombosis. Of the nonobstructive lesions, only varicose veins occur commonly. These are often the sequelae of the inflammatory reaction and obstruction of thrombophlebitis.

The following classification of the organic diseases of the veins shows their diversity.

### Organic Diseases of the Veins*

A. Obstructive
  1. Thrombophlebitis and phlebothrombosis (venous thrombosis)
     a) Local
     b) Primary
     c) Secondary
     (A more detailed classification appears in the section on thrombophlebitis)

Modified from the nomenclature prepared by the Nomenclature Committee of the Section for the Study of the Peripheral Circulation, the American Heart Association, 1941.

2 Neoplastic invasion of vein

3 Venous compression (with or without thrombosis or thrombophlebitis) due to gravid uterus neoplasm aneurysm, scar tissue, fractures and dislocations, shoulder neurovascular syndromes, increased intraabdominal pressure and extrinsic pressure due to tight girdles, circular elastic garters poorly fitted trusses *etc*

B Nonobstructive

1 Varicose veins
   a) Primary—congenitally incompetent valves
   b) Secondary to obstructive lesions or pressure
   c) Secondary to phlebitic destruction of valves
   d) Compensatory dilatation of collateral veins

2 Arteriovenous fistula—congenital traumatic, mycotic secondary to local disease

3 Aberrant position

4 Hypoplasia

5 *Phlebectasia*

6 Periphlebitis without thrombosis

7 Phlebosclerosis (not usually obstructive)

8 Rupture

## THROMBOPHLEBITIS

### (Phlebitis Phlebothrombosis Venous Thrombosis)

Thrombophlebitis is partial or complete occlusion of a vein by a thrombus associated with an antecedent or secondary inflammatory reaction in the wall of the vein ' Phlebitis ' is generally used synonymously in the literature although the term implies an inflammatory reaction without thrombosis

*Phlebothrombosis* has been popularized as a term by Ochsner and DeBakey and others to indicate a process in which the thrombosis is paramount and the inflammatory reaction mild or absent The thrombosis is due primarily to venous stasis and to those alterations in the cellular and fluid constituents of the blood which increase the clotting tendency *The distinction between* thrombophlebitis and *phlebothrombosis* is this in thrombophlebitis the clot is usually firmly attached to the wall of the vein and is unlikely to become detached in phlebothrombosis, the coagulum is poorly attached and may readily be broken loose to become an embolus The distinction, however is often difficult to make clinically, and clinically and pathologically, the result of the two is frequently the same Furthermore, embolism as the result of a fragment torn loose from the unattached tail of the thrombus in thrombophlebitis is not at all uncommon

*Etiology* —Thrombophlebitis often occurs immediately or shortly after a mechanical injury or as a complication of an acute illness In many cases, however, the condition arises without apparent reason The view held at present is that unexplained thrombophlebitis may occur as a consequence of one or more of the following initial lesions (1) a primary lesion in the wall of the vein involves the endothelium and gives rise to both inflammatory changes in the wall of the vein and to thrombosis within the lumen (2) thrombosis is primary and the result of venous stasis and other blood flow abnormalities that permit the platelets to adhere to the endothelium (3) thrombosis occurs as a result of alterations in the physicochemical properties of the blood that determine its coagulability In (2) and (3) the inflammatory reaction in the wall of the vein is secondary

THE ETIOLOGY OF THROMBOPHLEBITIS

I LOCAL THROMBOPHLEBITIS Changes in wall of vein are primary

A Chemical thrombophlebitis
   1 Result of injection of sclerosing solutions in treatment of varicose veins
   2 Result of injection intravenously of various drugs and diagnostic agents uch as the arsenicals antibiotic hypertonic solutions etc

B Local mechanical injury
   1 Secondary to contusions lacerations and fractures
   2 Axillary thrombophlebitis caused by strain or effort

C Local inflammatory thrombophlebitis (le ion essentially a part of a more extensive inflammatory process) as in erythema nodo um tuberculosis gummas granulomata and miscellaneous inflammations

1 Epidermophytosis (?) (probably by producing cracks in the skin which admit secondary invading organisms)

D *Suppurative thrombophlebitis*

1 Involvement of the wall of the vein by a suppurative process usually due to staphylococci streptococci or pneumococci

E Thrombophlebitis in varicose veins

1 Apparently spontaneous
2 Complicating infectious diseases
3 Postoperatively and post-partum

F Ischemic thrombophlebitis

1 Complicating acute arterial occlusion
2 Complicating *severe chronic occlusive* arterial disease

II Secondary Thrombophlebitis Thrombosis is secondary to underlying disease appears to be primary

A Post-partum thrombophlebitis

1 Milk leg (Phlegmasia alba dolens *puerperarum*)
2 Suppurative thrombophlebitis with pyemia

B Postoperative thrombophlebitis

C *Thrombophlebitis as a late complication* of severe injury

D Thrombophlebitis complicating infectious diseases

E Thrombophlebitis complicating blood dyscrasias such as chlorosis myelogenous and lymphatic leukemia polycythemia vera and anemia

F Thrombophlebitis complicating pregnancy

G Thrombophlebitis complicating noninfectious disease

1 Carcinoma especially visceral such as carcinoma of the pancreas of the lung and of the brain
2 *Heart disease*
  a Congestive heart failure
3 Diabetes *mellitus*
4 Gout
5 *Urinary lithiasis*

H Thrombophlebitis secondary to stasis due to

1 Prolonged dependency of limbs
2 Wearing constricting garments

III Primary Thrombophlebitis No evidence of predisposing systemic or local disease

A *Recurrent idiopathic thrombophlebitis* (thrombophlebitis migrans)

B Nonrecurrent idiopathic thrombophlebitis (essential thrombophlebitis)

## Pathology and Pathologic Physiology

*Pathology* —Although thrombosis and an inflammatory reaction in the wall of the vein *are common to all types of thrombophlebitis* the character of the thrombus and the extent of the phlebitis vary considerably *from case to case*

*The Thrombus* —A venous thrombus may be of three types (1) a red or coagulation thrombus *more or less homogeneous* and resembling a post mortem clot in which platelets and leukocytes are scattered rather evenly through a gelatinous mass of erythrocytes and fibrin (2) a white or agglutination thrombus in which the platelets and leukocytes are distributed in a laminated manner through the fibrin deposit in which very few erythrocytes appear (3) a mixed thrombus the commonest the head of which is white thrombus and the tail red thrombus or (more commonly) alternately red and white thrombus

A white thrombus is formed when venous stasis the development of eddy currents and perhaps a disturbance in the stability of the circulating blood platelets cause the platelets to migrate to the sluggish peripheral portion of the blood stream and become attached to the endothelial lining of the vein

This kind of thrombus is not solid the lamina extending in all directions divide and subdivide to form a honeycombed structure within the lumen The slowly moving blood stream is thus divided into numerous smaller streams In each of these the peripheral flow is slower than in the central *flow* hence more and more *platelets* and leukocytes are deposited on the existing lamina of the thrombus and further obstruct *and subdivide the blood stream* When the vein is completely or almost completely occluded there is sufficient obstruction to *produce* stasis of all or part of the stream A coagulation thrombus then forms proximal to the initial white thrombus Since occlusion *is not always complete* and interference with the venous flow is apt to be intermittent the tail of the thrombus frequently *consists of alternate sections of red thrombus* and white thrombus

A red thrombus alone forms when the *blood flow through a segment of a vessel* is brought to a sudden halt or marked venous stasis is combined with serious alterations

in the physicochemical properties of the blood that control coagulation

Where the injury or inflammation involving the endothelium is localized, the thrombus is also localized initially. Propagation of the tail of the thrombus may cause it to extend unattached, far into the proximal normal segment of vessel. A fragment may be detached and swept from the systemic venous circulation through the right side of the heart into the pulmonary circulation where it lodges as a pulmonary embolus

ring. In other instances, recanalization produces multiple small venous channels pursuing a tortuous and interconnecting course through a fibrous cord. When the valves of the veins are involved they are always damaged or destroyed

The inflammatory reaction in the wall of the vein varies in degree and in extent. It may be so slight as to involve no more than three layers of the wall, but the perivascular tissues as well (*periphlebitis*). During the early stages of thrombophlebitis *there is an infiltration by inflammatory cells*

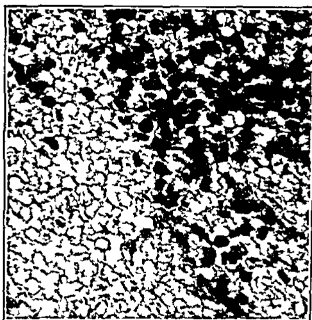


Fig. 181.—Fresh red thrombus composed entirely of erythrocytes. The hemolyzed erythrocytes are unstained. Photomicrograph. (Bell, Textbook of Pathology.)

Detachment of a portion of the tail is more common than detachment of the entire thrombus, especially if the tail has propagated as far as the junction of the involved vein and another large vein

Organization of the attached portion of a thrombus begins promptly with the growth of fibroblasts from the vessel wall into the thrombus. The organization progresses from the margin toward the center of the thrombus. In very large thrombi there is partial fibrosis and partial liquefaction. In some instances the result is the reestablishment of a *single* lumen, reduced in cross section and surrounded by a thick fibrous

leukocytes, lymphocytes and in increasing numbers fibroblasts

There is considerable variation in the pathological picture presented by the various types of thrombophlebitis. In chemical thrombophlebitis the thrombus tends to be adherent over a wide area and its organization is complete. The result is a cord-like fibrotic structure with a minimum of recanalization. Spontaneous thrombophlebitis in varicose veins is often almost purely a red thrombus which undergoes a protracted period of organization and involution. In suppurative thrombophlebitis the intense inflammatory reaction predominates. Col

lections of leukocytes and bacteria in the stroma become abscesses and these may communicate with the blood stream and so produce pyemia

In thrombophlebitis secondary to blood dyscrasias carcinoma and heart failure the inflammatory reaction is often minimal and it appears that the tendency to intravascular clotting in these instances is due largely to alterations in the coagulation mechanism of the blood and to venous stasis In primary idiopathic thrombophlebitis and in the thrombophlebitis secondary to thromboangiitis obliterans the lesions tend to be segmental and to involve the small and medium sized veins The inflammatory reaction is violent and is usually accompanied by considerable periphlebitis

The fibroblastic response is intense and is associated with endothelial proliferation which dominates the pathological picture occlusion appears to be due more to this than to thrombosis Giant cells may participate in the later stages of the reaction The usual result is obliteration of the vein which persists as a cord like structure Rarely is the lumen restored

There is great variation in the degree of the inflammatory reaction which occurs in secondary thrombophlebitis especially that which occurs postoperatively It is difficult to determine whether the thrombosis or the inflammation of the vein is the primary lesion The general view is that stasis and alterations in the coagulability of the blood are important factors in the production of this type of thrombosis

*Pathologic Physiology* —The essential physiological disturbance brought about by thrombophlebitis is obstruction of the venous flow in the involved vessels The degree of interference and its significance depends upon the size and the location of the involved veins and the extent of the thrombosis If only small superficial veins are involved the prognosis is good because of the rich collateral circulation and the numerous anastomoses present in most of the tissues of the body When major vessels are involved such as the iliofemoral or axillary veins obstruction by an extensive thrombus produces a marked rise in venous pressure in the distal portion of the affected limb

This causes intense congestion of the venules and capillaries and leads to transudation and edema There is disagreement about whether obstruction of the perivenous lymphatics plays any role in the early stages of edema formation Persistent chronic edema is probably due in part to such blockage which may persist because of perivascular fibrosis even after the venous channels have been restored by means of recanalization and the activation of collateral pathways

Vasospasm may contribute to venous obstruction during the acute stages of thrombophlebitis such vasospasm is analogous to the segmental arterial spasm that occurs in acute arterial occlusion

The obstructive process results in dilatation of collateral veins these are often overextended and owing to their relatively weak valves and walls tend to become varicosed Venous insufficiency results increased venous pressure producing further dilatation of the vessels and increasing stagnation When the important saphenous valve at the femoral vein is made incompetent in this way the entire venous pressure of the femoral and vena caval system is reversed and brought to bear on the relatively weak saphenous vein The orthostatic factor is very important in the pathologic physiology of the iliofemoral vein

SIGNS AND SYMPTOMS

1 *Pain* —The pain of thrombophlebitis may be slight as when a small segment of a superficial vein is involved or extremely severe as where a large venous trunk is involved It is sometimes local soreness or aching In iliofemoral thrombophlebitis it may be referred to the lumbosacral region and may simulate psoas abscess or spinal disease In patients with migratory thrombophlebitis the same type of local pain may involve venous branches throughout the body Periphlebitis produces relatively severe pain in thrombophlebitis effects of thrombosis are apt to overshadow the pain Pain in the calf produced by forced dorsiflexion of the foot (Homans sign) is sugges-

in the physicochemical properties of the blood that control coagulation

Where the injury or inflammation involving the endothelium is localized, the thrombus is also localized initially. Propagation of the tail of the thrombus may cause it to extend unattached far into the proximal normal segment of vessel. A fragment may be detached and swept from the systemic venous circulation through the right side of the heart into the pulmonary circulation, where it lodges as a pulmonary embolus.

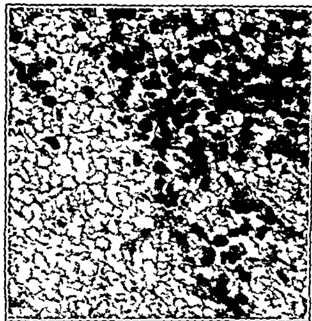


Fig 181 —Fresh red thrombus composed entirely of erythrocytes. The hemolyzed erythrocytes are unstained. Photomicrograph. (Bell, Textbook of Pathology.)

Detachment of a portion of the tail is more common than detachment of the entire *thrombus especially if the tail has* propagated as far as the junction of the involved vein *and another large vein*.

Organization of the attached portion of a thrombus begins promptly with the growth of fibroblasts from the vessel wall into the thrombus. The organization progresses from the margin toward the center of the thrombus. In very large thrombi there is partial fibrosis and partial liquefaction. In some instances the result is the reestablishment of a single lumen reduced in cross section and surrounded by a thick fibrous ring. In other instances recanalization produces multiple small venous channels pursuing a tortuous and interconnecting course through a fibrous cord. When the valves of the veins are involved they are always damaged or destroyed.

The inflammatory reaction in the wall of the vein varies in degree and in extent. It may be so slight as to involve no more than three layers of the wall, but the perivascular tissues as well (*periphlebitis*). During the early stages of thrombophlebitis there is an infiltration by inflammatory cells, leukocytes, lymphocytes and an increasing number of fibroblasts.

There is considerable variation in the pathological picture presented by the various *types of thrombophlebitis*. *In chemical* thrombophlebitis the thrombus tends to be adherent over a wide area and its organization is complete. The result is a cord-like *fibrotic structure with a minimum of recanalization*. Spontaneous thrombophlebitis in varicose veins is often almost purely a red thrombus which undergoes a protracted period of organization and involution. In suppurative thrombophlebitis the intense inflammatory reaction predominates. Col

on bilateral pressure There is usually a brawny swelling of the calf and an unusual prominence of the superficial vessels Pitting edema is not common and there are usually no constitutional symptoms

Any patient in bed after a major operation or a delivery or during a serious illness who complains of pain or tenderness in the calf should be suspected of having thrombophlebitis of the short saphenous muscular, or deep tibial veins

4) *Popliteal and lower femoral veins* Deep tenderness and pain occur along the course of the popliteal and the lower portion of the femoral veins There is usually rise and occasionally chills The temperature of the involved leg is usually unchanged but may be reduced if there is widespread arterial spasm There is tenderness in Scarpa s triangle and the thrombosed vein can be felt here There may be tenderness along Hunter s canal and into the popliteal space

The diagnostic triad for this condition follows diffuse enlargement of the limb congestion of the skin and superficial veins and tenderness in Scarpa s triangle In addition it is very helpful to be able to feel the cord like thrombosed vein

TABLE 55 —THE DIFFERENTIAL DIAGNOSIS OF ACUTE ILIOFEMORAL THROMBOPHLEBITIS ACUTE ARTERIAL OCCLUSION AND ACUTE LYMPHANGITIS WITH CELLULITIS

| | *Acute Iliofemoral Thrombophlebitis* | *Acute Arterial Occlusion* | *Acute Lymphangitis with Cellulitis* |
|---|---|---|---|
| Size of the limb | Enlarged | Unchanged or shrunken | Enlarged |
| Color of the limb | Normal or slightly cyanotic | Pale initially later may be mottled cyanotic | Red |
| Skin temperature of the limb | Usually normal | Low | Elevated |
| Superficial veins | Prominent and distended | Collapsed | Usually unaffected |
| Arterial pulsations | Usually normal | Absent | Normal |
| Chills | Unusual | Absent | Usual at onset |
| Fever | Rarely more than 102 F | Usually absent | Usually high 103 to 104 F |

swelling and congestion of the lower leg Mild constitutional symptoms are common The cord like thrombosed vein can often be palpated

5) *Iliofemoral Thrombophlebitis* The onset is usually sudden but may be preceded by evidence of a more distal thrombophlebitis or by pulmonary embolism The pain is moderate or severe and may extend from above Poupart s ligament down the course of the involved vein to involve the entire leg There is often diffuse pain The superficial veins are somewhat prominent and distended and the skin may be diffusely or locally cyanotic Ordinarily there is significant enlargement of the entire involved extremity Constitutional symptoms are usual fever usually tachycardia and mal

The swelling of the limb is often brawny and firm initially and the skin over the tibia may not then pit on pressure As congestion subsides pitting edema may appear Constitutional symptoms persist for anywhere from a few days to three weeks Before anticoagulant treatment they often lasted for months The tenderness in Scarpa s triangle is ordinarily the last sign to disappear Its disappearance indicates that complete involution has occurred

6) *Axillary brachial or subclavian veins* The picture is much like that presented by iliofemoral thrombophlebitis The thrombosed axillary or brachial vein can readily be felt as a cord There may be intense congestion and considerable cyanosis of the whole arm

tive of thrombophlebitis (phlebothrombosis) of the deep veins of the calf But this is not an infallible test, injuries and inflammations of the muscles and nerves of the calf may cause the pain

2 *Tenderness* —There is usually tenderness along the involved veins, this is diffuse when the deep veins are involved, acute and localized when superficial veins are involved (*e g*, in Scarpa's triangle, Hunter s canal, the popliteal space and in the axilla)

3 *Cramps* —Severe muscular cramps not infrequently occur in cases of phlebitis of deep vessels especially the deep veins of the calf The danger of embolization is increased during the cramps due to the contraction of the muscles upon the thrombosed veins

4 *Color Changes* —Superficial thrombophlebitis is almost always accompanied by redness of the skin over the involved vein This redness may extend either as a red streak along the involved vein or as diffuse patches from the site of involvement With migratory thrombophlebitis such patches appear in each area of involvement As the acute process subsides the patches fade Occasionally, the periphery of an extremity involved by thrombophlebitis becomes blanched or cyanotic this is due to associated vasospasm Gangrene may occur as a result of arterial spasm Pallor may also be prominent in cases of milk leg if lymphatic obstruction is a major factor

5 *Local Swelling* —Mild or moderate local swelling is usually associated with thrombophlebitis When the involved vein is superficial, a lump or a cord like mass is palpable along its course When a deep vein is involved, this lump is often not discovered

6 *Edema* —Thrombosis is accompanied by some degree of congestion throughout the venous system and capillary bed distal to the point of thrombosis There may not be any gross edema This is especially apt to be the cause if the involved vein is superficial and the collateral circulation is adequate But in about half the patients gross edema does occur It is greatest when the large venous trunks especially the femoral iliac, are involved, along with the lymphatic vessels This causes the condition known as phlegmasia alba dolens, or milk leg

7 *Fever* —Fever may or may not be present As a rule there is moderate fever of from 100 to 102° F (from 37 7 to 38 8° C) In rare cases it may be much higher

8 *Tachycardia* —Rapid pulse is common even when there is no fever Persistent tachycardia unexplained on another basis is evidence of continued thrombophlebitic activity

## Laboratory Findings

*Sedimentation Rate* —The sedimentation rate is unpredictable in acute thrombophlebitis, the range is wide but is said to parallel roughly, the degree of fever If the sedimentation rate is high it is probably unwise to permit the patient any activity

*Blood Count* —The leukocyte count may or may not be affected by thrombophlebitis Ordinarily there is no anemia

## Common Sites for Thrombophlebitis

1) *Superficial veins tributaries of the saphenous system, or small cutaneous veins* These vessels are often involved by multiple lesions which appear as red moderately painful and tender raised areas in the skin As a rule the lesions are linear and feel like small cords along the course of the visible vein Constitutional symptoms are rare The inflammatory reaction undergoes involution in from one to three weeks but a firm thrombosed segment of vein can be felt for a much longer period There may be extension to larger vessels

2) *The long and short saphenous veins the median basilic vein and the cephalic vein* Since these veins are large and superficial and are usually involved by periphlebitis the affected vein can ordinarily be felt as a firm cord Edema is uncommon but may occur in the leg if the process is severe and the patient remains ambulatory during the acute stage Constitutional symptoms are usually mild or absent

3) *Muscular veins and deep veins of calf* Thrombophlebitis of the calf veins (phlebothrombosis) causes pain in the calf and tenderness of the calf muscles particularly

to anticipate this complication. Prophylactic therapy, whether pulmonary embolism has occurred or not, includes the institution of anticoagulant therapy.

If a warning embolus is present, heparin and Dicumarol* should be administered immediately; otherwise it is enough to give Dicumarol* alone. New anticoagulants including Tromexan, Paritol and Phenyl-indandione are being studied at present.*

Ligation of the femoral vein for femoral thrombophlebitis, of the iliac vessels or inferior vena cava for iliofemoral thrombophlebitis, and of the long saphenous vein for thrombophlebitis involving this vein are not ordinarily desirable. Venous ligation as a prophylaxis against pulmonary embolism is inferior to anticoagulant therapy because:

(1) acute thrombophlebitis is less apt to produce pulmonary embolism than is phlebothrombosis of the deep vessels; (2) fatal pulmonary emboli arise from sites not recognized during life and therefore not likely to be selected for ligation; (3) venous ligation does not always prevent pulmonary embolism, which may arise from a point proximal to the ligation; (4) anticoagulant therapy is a more effective means of preventing pulmonary embolism. Even if ligation is performed, it should be followed by the administration of anticoagulants.

Ligation of the iliac veins or inferior vena cava is indicated in rare instances, as when thrombophlebitis progresses rapidly despite anticoagulant therapy, when blood dyscrasias tending towards hemorrhage exist, or when there are bleeding or ulcerated mucous membranes. Venous ligation may also be indicated when there is serious liver or kidney disease, or following multiple pulmonary emboli arising from phlebitis in the leg. Lastly, ligation may be used when properly controlled anticoagulant therapy is not available.

*Treatment of Pulmonary Embolism.*—Treatment for small pulmonary emboli includes anticoagulant therapy, the administration of opiates to control pleural pain, and rest in bed until all symptoms and signs have subsided (ordinarily a matter of a week). Anticoagulants should be continued for 3 or 4 weeks after the embolic episode.

Large emboli, such as those producing acute cor pulmonale and shock, call at once for emergency measures. The patient is placed in an oxygen tent and given 50 mg. of heparin, 30 mg. of papaverine and 0.6 mg. of atropine sulfate intravenously. Heparin is continued until Dicumarol* has been given long enough to obtain therapeutic prolongation of the prothrombin time. The patient is kept warm, pain is controlled by codeine or morphine, and papaverine is given every four hours until the acute phase has subsided. The patient is kept in bed until all signs and symptoms have subsided, but anticoagulant therapy is continued for from 3 to 4 weeks.

Shock is combatted by all appropriate means, including blood transfusion, which should be delayed until heparin has been administered. Regardless of the dose of heparin already given, an additional 50 mg. should be given immediately after the transfusion.

*Prevention of Sequellae.*—To avoid the development of chronic venous insufficiency, the patient with moderate-to-severe thrombophlebitis of the leg should not be permitted out of bed until fitted with a knee-length elastic stocking to be worn while he is ambulatory. This stocking should be fitted when the leg is free from edema. It is applied to the leg before the patient leaves his bed and is worn during the entire day; it may be removed when the patient is able to rest in bed with his leg elevated. For the sake of comfort, it may be removed once or twice a day for a short time. After a period of from three to six months, the elastic support may be discarded for half a day to see whether edema appears.

If it does, the stocking is worn for another month, after which the leg is tested again. When the patient can remain ambulatory for half a day without the elastic support and without developing edema, he may try to go a whole day without the support. The stocking may be discarded only when no edema or feeling of heaviness appears in its absence.

* The administration of pellets of heparin by sublingual route is effective; it is an easy and practical way to administer this anticoagulant (Proc. Soc. Exp. Biol. and Med., June 1951).—Editor.

TREATMENT

*Prophylactic.*—Prophylaxis depends on successful management of predisposing diseases, prevention of trauma and venous stasis, and maintenance of normal hemostasis. One attack of thrombophlebitis is likely to lead to other attacks. Thrombophlebitis secondary to thromboangiitis obliterans, a blood dyscrasia or an infectious disease is less apt to occur when the primary disease is controlled. In the presence of congestive heart failure, venous stasis and hypercoagulability of the blood, anticoagulant therapy reduces the risk of venous thrombosis.

Preventive measures for debilitated patients or patients bedridden as a result of major surgery, instrumental or complicated deliveries, or serious illness should include (1) frequent deep breathing exercises, (2) passive and active exercises of the feet and legs, (3) massage of the legs, (4) adequate hydration, (5) adequate treatment of infection, (6) early ambulation, (7) maintenance of optimal environmental temperature, and when the risk of venous thrombosis is great, (8) anticoagulant therapy. Additional measures in surgical, obstetrical and accident cases should include (1) meticulous surgical technique, (2) avoidance of pressure on legs during and after surgery, (3) avoidance of excessive abdominal and inguinal compression from dressings, and (4) maximum care in intravenous therapy (to avoid excessive injury and the infiltration of surrounding tissues).

Venous thrombosis after prolonged dependency and immobilization of the legs during travel by plane, train, bus or automobile can be avoided by periodic exercises and by not wearing circular garters or other constricting garments (*e. g.*, girdles).

*Active.*—The legs of bedridden patients should be examined daily for signs of thrombophlebitis. Early therapy is imperative if phlebothrombosis, which may present the most innocuous local effects but result in pulmonary embolism, is to be controlled promptly.

Rest, heat, elevation and the use of anticoagulants are fundamental in the treatment of thrombophlebitis. Localized superficial thrombophlebitis will ordinarily respond promptly to elevation of the leg or arm and the application of warm, moist packs to it. The packs should extend the full length of the leg or arm and be applied for 20 hours out of each 24 until all tenderness has disappeared, usually in 5 to 10 days.

Instructions for applying packs: Anoint the skin with protective oil or grease and cover with a single layer of gauze. Dip pieces of flannel or turkish towels in boiling water, wring nearly dry, and apply to the entire limb. Be careful not to burn the skin. Wrap a rubber cloth around the flannel and a heavy bath towel around the rubber cloth. Hot-water bottles may be applied outside the bath towel. Moist heat is more effective than dry heat and is less apt to burn the skin.

Pain may be controlled by the use of sedatives or opiates. In 3 or 4 days the patient can usually move the affected leg or arm comfortably. He should then exercise his toes and feet and shift his position frequently. Until the inflammation has subsided, more vigorous motion will cause distress. When pain, tenderness and swelling have subsided and the patient's temperature has been normal for 24 hours, the packs may be discontinued and the patient gradually allowed to become ambulatory. This will ordinarily require from 7 to 14 days. In instances of axillary or subclavian thrombophlebitis the treatment is the same, but the patient may sit in a chair after the first 4 or 5 days if the affected limb can be kept elevated.

Lumbar sympathetic block is indicated when thrombophlebitis is accompanied by marked vasospasm. Ordinarily, moderate vasospasm will respond to heat, elevation, rest, and sedatives or analgesics. In cases of severe vasospasm, sympathetic blocks should be performed on each of the first 2 or 3 days.

*Prevention of Pulmonary Embolism.*—Pulmonary embolism is theoretically more apt to result from phlebothrombosis of the deep veins of the plantar region or the calf than from acute thrombophlebitis. But fatal pulmonary emboli may result from inflammatory thrombophlebitis at any time, and it is beyond the ability of the physician

especially when the long saphenous system is involved The venous flow may actually be reversed so that the blood flows away from the heart through this system (retrograde flow) and from the deep veins through the communicating veins into the long saphenous vein Pooling of blood in the peripheral venous channels causes edema anoxia, and accumulation of metabolic wastes and results in local tissue damage

### Symptoms

The symptoms arising from varicose veins are more often due to chronic venous insufficiency and stasis than to the veins themselves

Extensive varicose veins may, in themselves produce few symptoms Some patients with minimal varicosities may on the other hand present numerous complaints When symptoms appear out of proportion to the extent of the varicosities and the degree of venous insufficiency, other causes for the complaints must be sought—*e g* arterial insufficiency, sciatic pain chronic foot strain fibrositis arthritis, chronic nervous exhaustion or psychoneurosis Frequently moderate or even sharp pain may occur while a varicosity is developing

The most common symptoms are fatiguability of the leg muscles a sense of fullness and congestion in the leg soreness in the region of the varicosities muscular cramps (especially nocturnal) and paresthesias (burning pain and itching) Localized eczematoid dermatitis may develop and lead to pigmentation especially if there has been injury to the skin through scratching Women often complain of the appearance of the varicosities and may have subjective complaints out of proportion to the degree and extent of the venous involvement

### Signs

A complete physical examination should be made of patients with varicose veins treatment depends on the presence or absence of constitutional disease infection peripheral arterial disease abdominal tumor or edema and chronic venous insufficiency which may have resulted from old thrombophlebitis Examination of the veins should be made while the patient is standing on a platform and facing a good light Palpation is often of greater value than inspection

The following tests are used for testing the competency of the saphenous veins

*Brodie Trendelenberg Test* —Blood is drained from the superficial veins of the patient s leg by having the patient lie down and raise his leg The upper portion of the saphenous vein is then obstructed with the fingers and the patient asked to stand Rapid filling while pressure is maintained indicates valve incompetency of the communicating veins As the pressure of the fingers is lifted, rapid filling from above indicates valve incompetency of the saphenous vein Slow filling from below both while pressure is exerted and when it is released is normal

*Perthes Test* —The long saphenous vein is compressed by a tourniquet on the thigh and the patient made to walk briskly Normally the return venous flow is aided by the walking the flow being from the superficial to the deep veins Normally, too the veins disappear rather rapidly thus indicating competent communicating veins If the veins do not disappear, the communicating veins are incompetent, if the veins become more prominent and discomfort or pain occur upon walking, the communicating veins are incompetent and the deep veins obstructed

*The Bandage Test* —The leg is wrapped from toe to knee with a heavy rubber bandage tight enough to compress the superficial veins but not so tight as to interfere with the arterial blood flow

The patient should be comfortable while recumbent He is then asked to walk briskly for 30 minutes If he can do so without discomfort the deep veins are patent Pain on walking indicates obstruction of the deep venous channels and a need to preserve the superficial veins It should be remembered that arterial insufficiency may cause pain under these conditions and should therefore be ruled out before the test is performed

### Diagnosis

The diagnosis of varicose veins is ordinarily not difficult Since varicosities

During the first 4 to 8 weeks after thrombophlebitis, the patient should sleep at night with the foot of his bed elevated 8 or 10 inches. Later, he should exercise his leg regularly by means of bicycle exercises in bed and by swimming. Prolonged rest in bed after thrombophlebitis is inadvisable because of the danger of muscular atrophy and osteoporosis and in apprehensive patients neurosis. When the acute process has subsided, these may be prevented by gentle passive and active exercise in bed and by early ambulation. Post-phlebitic neuritis, while uncommon, may be managed by the single or repeated block of the involved nerve with novocaine. Active motion of the leg and an encouraging attitude on the part of the physician are important in preventing or ameliorating these complications.

## VARICOSE VEINS

(Phlebectasia, Venous Aneurysm)

Varicose veins are simply dilated veins. The term may be used to describe all dilated veins except those which are dilated as a result of arteriovenous fistula or as a part of a vascular tumor.

### Etiology

Primary varicose veins develop spontaneously, presumably as the result of a hereditary weakness of the walls and/or the valves of the veins. Because of this weakness, the veins are unable to withstand the increased pressure which results from such factors as orthostatism (prolonged standing), increased abdominal or pelvic pressure (abdominal obesity, pregnancy, large intra-abdominal tumors), or external pressure (constricting garters and girdles).

Secondary varicose veins are ordinarily a late complication of thrombophlebitis, most commonly iliofemoral thrombophlebitis. The thrombophlebitic process damages and destroys the walls of the vein and the valves not only of the involved vein but of the communicating veins between the deep and superficial systems as well. Secondary varicose veins may develop in the absence of hereditary predisposition to varicose veins if the venous pressure is increased significantly by obstruction.

The frequent appearance of varicose veins in women during pregnancy is explained largely on the basis of an increase in the venous pressure in the legs. The mechanism for the increased pressure is presumed to be a combination of the following factors: pressure of the uterus on the iliac veins, increased intra-abdominal pressure, and increased venous blood flow from the internal iliac veins into the common iliac vein.

### Incidence

Varicose veins are exceedingly common among the general population. They occur at all ages and with considerable frequency after the age of twenty, more commonly in women than in men.

### Pathology

The essential pathological changes in varicose veins are (1) dilatation of the veins, (2) elongation and increased tortuosity, (3) fibrosis and loss of elasticity, (4) irregular thickening (usual) or thinning (unusual) of the walls of the veins as a result of muscular hypertrophy and subintimal and interstitial fibrosis, and (5) atrophy and destruction of the valves.

Incompetency of the valves is believed to be largely secondary to the dilatation of the vein; the valves, however, may be involved in the destructive inflammatory process leading to dilatation. At any rate, dilatation of the veins leads to valvular incompetence, which, in turn, predisposes to further progressive dilatation of the involved vessels.

Varicosities occur most commonly in saphenous veins and their tributaries. The communicating veins between the superficial and deep systems are frequently involved. Involvement of the superficial cutaneous veins is very common. The deep veins are less often involved.

The venous pressure is usually but not always elevated in varicosed veins. This pressure is elevated dramatically even in normal veins of the legs when a person changes from the recumbent to the erect position. More important than the venous pressure is the marked change in blood flow

appear until orthostatism has added its burden to the pressure on the tissues. As it progresses *the edema is complicated by cyanosis, congestion, pigmentation and sometimes purpura and petechiae.*

*Dermatitis or eczema commonly occur.* The eczema may be dry and scaling or moist and weeping. Intense pruritis may lead to persistent scratching.

The longer the edema exists, the greater *is the subcutaneous fibrosis.* Eventually the swelling does not disappear upon recumbency. Often a low grade inflammatory process supervenes, leading to chronic indurative cellulitis. The patient is then prone to develop all the serious complications *inherent in this type of lesion: lymphangitis, erysipelas,* ulceration.

Ulceration is common and serious in chronic venous insufficiency. It develops where the nutrition of the skin is most impaired, particularly where trauma has increased the local insult. It may occur anywhere at the site of chronic induration *or eczema, most commonly in the region of* the ankles, above and below the malleoli. Ulcers may be of any size and shape and tend to become chronic if the patient remains

TABLE 56.—THE DIFFERENTIAL DIAGNOSIS OF CHRONIC VENOUS INSUFFICIENCY

| *Condition* | *Features Which Differentiate Condition from Chronic Venous Insufficiency* |
|---|---|
| | I. CONDITIONS PRODUCING SWELLING OF THE LEG |
| *Congestive Heart Failure* | Edema is usually *bilateral and symmetrical,* often present elsewhere. *Is* usually accompanied by other evidence of heart failure |
| *Chronic Nephritis (Nephrotic Syndrome)* | *Edema is soft, pale, pitting, bilateral, symmetrical and occurs elsewhere.* Urinary findings and history clarify diagnosis |
| *Chronic Lymphedema* | *More diffuse induration without venous congestion or dilated veins.* Edema is pale. Subsides slowly if at all upon recumbency and elevation. No dis*tension and dilatation of superficial venules* |
| Arteriovenous Fistula | History of penetrating injury or presence since birth. Presence of thrill and *bruit not invariable. Increased length of limb and dilated veins in unusual* locations and distribution. Oxygen saturation of venous blood is increased |
| | II. CONDITIONS PRODUCING PAIN IN THE LEG |
| Intermittent Claudication (Muscle Ischemia) | Pain develops only during muscular activity, is relieved by rest without elevation. Evidence of arterial insufficiency |
| Tumors of the deep structures of the leg | Uncommon. Usually in upper calf. *Irregular structure.* Bone tumors differentiated on x-ray |
| Abscesses | Uncommon. Site may be unrelated to vein. Signs of acute inflammatory process |
| *Myositis* | Uncommon. *Absence of superficial induration and cutaneous changes.* Absence of venous disease |
| | III. CONDITIONS PRODUCING INDURATION OF LEG |
| Scleroderma | Commonly involves digits. Absence of venous disease. May present peripheral arterial disease. Upper extremity more commonly involved |
| Tumors | Uncommon, *see above* |
| Acute Cellulitis | Acute onset and evidence of acute inflammatory process. Etiology other than venous insufficiency |
| | IV. CONDITIONS PRODUCING ULCERATION OF LEG |
| Hypertensive-Ischemic leg ulcers | Long standing or severe hypertension. Commonly peripheral arterial disease. Absence of venous disease. Very rare |
| Syphilitic ulcers | Tend to form on upper portion of leg, to be multiple and to form a pattern. Begin as nodules, ulcerate and heal with atrophic scars. Serological tests helpful |
| *Arterial insufficiency* | Most common on toes and feet. *Usually painful.* If on leg, usually follow trauma. Other signs of arterial insufficiency but not those of venous insufficiency |
| Ulcerative tuberculids | Usually bilateral and symmetrical. May occur elsewhere. *Painful nodules which ulcerate and resist therapy* |

not uncommonly follow obstruction of the veins proximally, such obstructions should be sought and removed, if possible. Occasionally, varicose veins arise secondary to arteriovenous fistula; this may be suspected when varicosities have existed from birth or have followed trauma, particularly penetrating injury.

### Complications

The complications of varicose veins are thrombophlebitis and chronic venous insufficiency. Chronic venous insufficiency is manifested by cyanosis, edema, acute or chronic induration and cellulitis, necrosis, ulceration, eczema, and pigmentation of the skin.

### Treatment

*Conservative Treatment.*—The conservative management of varicose veins is indicated for patients with early, mild varicosities and for those in whom more active therapy is contraindicated. The measures employed are (1) adequate periods of rest with the feet and legs elevated; (2) avoidance of unnecessary standing and walking; (3) avoidance of external constrictions about the legs and hips (girdles, garters, *etc.*); (4) support of the legs by elastic bandages or stockings. This type of management is useful for many cases, especially during pregnancy.

*Injection Treatment.*—Injection treatment may be done alone or in combination with surgical ligation or extirpation of the veins. Satisfactory results are obtained by injection alone only when performed on small superficial varices (telangiectatic spider bursts) or on localized varices not associated with any general incompetency of the saphenous systems.

The results of injection therapy for large varicose veins are usually disappointing, the varices tending to recur within a year or two.

*Surgical Treatment.*—The techniques of venous ligation, of retrograde injection and of excision of veins are beyond the scope of this discussion. Severe varicosities associated with incompetency of the great or small saphenous systems must be treated surgically if permanent improvement is sought. The procedure usually consists of dividing the greater saphenous vein at the saphenofemoral junction and either injecting the distal segment of the vein immediately with sclerosing solution or excising the vein through multiple small cutaneous incisions.

In patients with severe varicosities in the short saphenous system, this vein may be ligated and divided in the popliteal space. Small and localized residual varicosities remaining after operation may be obliterated by injection. It is often necessary to ligate individually the bulging superficial ends of the communicating veins to produce a satisfactory result.

## CHRONIC VENOUS INSUFFICIENCY

(Venous Stasis, Stasis Edema, Stasis Eczema, Stasis Ulcer, Varicose Ulcer, Postphlebitic Ulcer.)

Chronic venous insufficiency is a localized or generalized pathological state of the tissues, usually of the legs, resulting from stasis of the venous blood flow. Stasis is usually caused by obstruction of a venous trunk, particularly the iliofemoral. The obstruction results from thrombophlebitis, neoplastic invasion, continued extrinsic pressure, incompetence of the valves of the iliofemoral vein through destruction by thrombophlebitis or old and extensive varicosities.

In venous stasis the venous blood is deficient in oxygen and contains an excess of carbon dioxide and protein metabolites. Increased venous pressure and slowing of the venous stream result in abnormal function of the venules and capillaries. Failure of the reabsorption mechanism leads to edema. A vicious cycle is set up which manifests itself in fibrosis, induration, cellulitis, pigmentation, necrosis and ulceration. These changes result from pressure, congestion and poor nutrition.

### Symptoms and Signs

The first manifestation of chronic venous insufficiency is subcutaneous edema which responds to bed rest. Other signs do not

mount importance is control of the edema If, on fair trial ambulant therapy does not bring about healing of stasis ulcer the patient must be put to bed

After a stasis ulcer heals, the patient must wear an elastic support for a long time, often for a year sometimes permanently Areas of ulceration on which pressure is not exerted by an elastic support must be covered with a sponge or molded latex pad beneath the elastic bandage or stocking Ulceration is apt to recur if venous stasis is not controlled and trauma prevented

## HYPERTENSIVE-ISCHEMIC LEG ULCERS

Otherwise unexplained ulcers on the leg may be the so-called hypertensive-ischemic leg ulcers well described by Hines and Farber in 1946 In some cases of hypertension the arterioles of the skin become occluded and small areas of skin are infarcted When these infarcted areas break down an ulcer is formed Most hypertensive-ischemic ulcers described in the literature have been in the region of the ankle

Clinically, a painful red plaque appears, becomes cyanotic and then purpuric The small area of discoloration develops into a hemorrhagic bleb which breaks down to form a superficial ulcer The ulcer enlarges slowly to reach a size of from 1 to 7 cm Healing is protracted, since granulations form slowly and there is only slight exudation Pain is often quite severe

Pathologically there is thickening of the walls of the cutaneous arterioles and a proliferation of the intima which narrows the lumen There is hyperplasia of the media with hyaline degeneration and a perivascular reaction

## CRANIAL ARTERITIS

### (Temporal Arteritis)

Cranial arteritis is a febrile self limited inflammatory disease of variable duration and unknown etiology involving the temporal and often other arteries of the cranial system It chiefly occurs in persons over fifty

### Etiology

The character of this debilitating but subacute condition suggests that it may be due to a low grade infection Indeed focal infection has been suggested as the cause extraction of the teeth having resulted in improvement in a few cases Attempts to explain the disease on an allergic basis have also been made but these are scarcely convincing for the disease is highly localized, eosinophilia is not ordinarily a feature, and the patients are almost always elderly Though the lesions of cranial arteritis may sometimes resemble those of periarteritis nodosa pathologically the two conditions are so different in clinical course that it seems impossible that they should be closely related

### Pathology

The larger temporal arteries become tortuous nodular, and swollen Pulsations may be present or they may be absent as a result of nodulation or thrombosis There may be cellulitis of the surrounding tissues Facial carotid occipital cerebral and retinal arteries may be involved Microscopically panarteritis with hypertrophy of the intima necrosis of the media and granulomatous changes (often showing giant cells) in the vascular walls may be observed Externally periarterial cellular infiltration of the affected vessels occurs internally thrombosis is common Eosinophilic lesions rarely occur

### Symptoms and Signs

*Cerebral symptoms* include headache vertigo nausea vomiting mental sluggishness and confusion delirium and rarely coma *Ocular symptoms* include photophobia various degrees of blindness ptosis and retinal changes *Systemic symptoms* usually severe include fever, malaise, anorexia weight loss sweating and weakness *Local signs* depend on the degree of inflammation and induration Pulsations in the temporal arteries are abolished when thrombosis occurs or when diffuse induration or nodulation are advanced Periarterial cellulitis may supervene

ambulatory. We have seen ulcers of more than 35 years' duration. Infection is common. Ulcers do not ordinarily occur on the upper leg or on the feet.

Pain is produced by a variety of causes in chronic venous insufficiency. On walking there is a dull ache, due to the stasis and congestion; this pain is usually relieved by recumbency and elevation of the leg. Arthritic pains are often aggravated in a leg with chronic venous insufficiency. Nocturnal musclar cramps may occur from venous insufficiency. Pain due to ulcers and indurative cellulitis may be severe though usually relieved by rest and elevation. Neuritis of the nerves supplying the long saphenous vein and other tissues occasionally occurs.

## Treatment

The patient with chronic venous insufficiency should stay in bed with the affected leg elevated until all edema has disappeared and should be made to wear an elastic stocking or bandage before leaving bed. This support, which the patient should wear at all times while he is ambulatory, should extend from toe to knee, but not above the knee. Even though equipped with such a support, the patient should avoid unnecessary walking or standing. The foot of his bed should be elevated at least 6 inches from the floor at night so that the veins and tissue spaces of the affected leg will tend to drain. Superficial varicose veins should be ligated, injected, or both, if the deep veins are competent.

Epidermophytosis should be treated by soaking in 1:5000 to 1:10 000 potassium-permanganate solution once or twice daily for 30 minutes. Fungicidal dusting power may also be used, but strong fungicides should not be used on devitalized tissues.

Eczema will improve as stasis is overcome, but symptomatic measures are necessary for pruritis. If an elastic support cannot be tolerated because of itching, pain or oozing, the patient should be kept in bed. Local measures for subjective relief include the application of 3 per cent ichthyol in zinc-oxide ointment, wet dressings of 0.5 per cent aluminum subacetate, or 0.01 per cent potassium permanganate. A satisfactory antipruritic is 10 per cent ethyl aminobenzoate ointment (benzocaine, anesthesin).

Cellulitis requires bed rest, elevation of the limb, and the application of warm, moist dressings. If the condition is spreading or producing a systemic reaction, antibiotic or chemotherapeutic treatment is indicated. If the cellulitis is chronic and advanced, improvement may take several weeks.

Purpura and petechial hemorrhages due to capillary rupture are secondary to increased venous pressure and local nutritional deficiency. The addition of 300 mg. of vitamin C to the daily diet of patients so afflicted is desirable.

The presence of stasis ulcer calls for bed rest and elevation of the limb until edema has subsided. If clean, the ulcers are exposed to the air; if infected, they are treated with wet dressings of penicillin or tyrothricin. Local varicosities should be ligated promptly, if possible, to prevent the retrograde blood flow which often prevents healing of the ulcer. The skin around the ulcer should be protected with a bland and soothing ointment. Healing of bacteriologically clean ulcers appears to be accelerated in some cases by the daily application of dried human erythrocytes (Lyocyte powder).

When edema has subsided, compression may be applied to the area of ulceration by binding on sterile rubber sponges, or applying elastoplast bandages, or even an Unna paste boot. The healing of clean ulcers is accelerated by the application of split thickness skin grafts.

Since many patients with ulcers cannot or will not stay in bed long enough for the ulcer to heal, proper management of the condition on an ambulatory basis is important. If possible, the patient should be kept in bed until edema has subsided.

For the ambulatory patient, the ulcer is cleansed and covered with sterile Vaseline gauze. Pressure is exerted over the area by the application of a piece of sponge rubber somewhat larger than the ulcer. This is held in place with a piece of elastoplast bandage. Elastic support to the leg is provided by means of an elastic bandage or stocking or an Unna paste boot. Of para-

lymph system are lymphatic fistula, chylous ascites due to obstruction of the thoracic duct, and obstruction due to fibrosis and calcification.

## LYMPHEDEMA

Lymphedema is a swelling of the soft tissues which is due to an increased quantity of lymph in the tissue spaces. The term *elephantiasis* implies an enormous swelling of the legs without indicating the cause. A simple and convenient classification of the causes of lymphedema follows:

ETIOLOGICAL CLASSIFICATION OF LYMPHEDEMA (OBSTRUCTIVE NON-INFLAMMATORY DISEASE OF THE PERIPHERAL LYMPH VESSELS)

1. *Primary lymphedema*
   - a. Congenital (simple) lymphedema
   - b. Hereditary lymphedema (Milroy's disease)
   - c. Lymphedema praecox
2. Secondary lymphedema due to
   - a. Surgical removal of lymph nodes
   - b. Neoplastic invasion of lymph nodes
   - c. X-ray treatment

### ETIOLOGY

The mechanism of lymphedema is always the same regardless of the primary cause. Obstruction of the lymph flow by inflammatory or non-inflammatory processes causes stasis, increases lymph pressure, and produces dilatation of the vessels. Dilatation of the vessels produces insufficiency of the valves and so eliminates one of the two important factors assisting the flow of lymph. Obstruction furthermore causes the lymph to seek other channels than those normally used. The protein content of the lymph increases; fibroblastic proliferation then leads to fibrosis and further stasis. An increase in protein-rich extracellular fluid predisposes to attacks of acute inflammation which in turn produce thrombosis of the lymphatics, further lymph stasis, and further fibrosis.

### INCIDENCE

Primary lymphedema occurs chiefly among women and usually during the second or the third decade of life. The involvement is unilateral in about 70 per cent of the cases. The congenital form is evident at birth or soon afterwards. Milroy's disease is the familial form. The secondary forms of lymphedema are relatively uncommon.

### PATHOLOGY

The characteristic pathological picture of congenital lymphedema includes thickening of the subcutaneous tissues and replacement of the adipose tissue with enlarged lymph spaces and connective tissue. There are no thromboses of lymphatics or blood vessels and no inflammatory changes.

Other types of lymphedema are characterized by thickening of the skin and subcutaneous tissues (with replacement of the adipose tissue by lymph channels and connective tissue), atrophy of muscles, nerves, and sweat glands, and infiltration of the tissues by lymphocytes, leukocytes, and other cells.

### CLINICAL SIGNS

*Lymphedema Praecox.*—This type of lymphedema occurs spontaneously, usually at puberty or during adolescence. The first sign is a slight puffiness around the foot or ankle. This is frequently more pronounced during long periods of activity, during menstruation, and in warm weather.

Rest in bed with elevation of the limb produces temporary disappearance of the edema. One or both limbs may be involved, or one may be involved months after the appearance of the edema in the other limb. The edema may progress up the leg either rapidly or slowly. In a few cases the swelling does not progress beyond the ankle or beyond the knee.

The edema becomes progressively more severe and, though reduced through rest and elevation, reappears upon activity and dependency. The skin becomes roughened and the edema more resistant to pressure. Hypertrophy of the soft tissue results in a large, uncomfortable, and unsightly limb. The patient may feel a sense of heaviness in the limb, but pain does not occur. Inflammatory reactions are uncommon and ulceration does not occur. Since only the lower limbs are involved, gravity is thought

### Course

The onset is usually insidious, the patient may suffer constitutional disturbances for weeks or months before the focal symptoms appear. There are usually fever, sweating and vague generalized aching. Progressive weight loss may be dramatic. Headache develops, usually over the involved vessels. Pain may radiate to the occiput, the jaw, the sides of the head, or to the face. Pain may limit the movement of the jaws and interfere with eating.

The cervical lymph nodes may be enlarged and tender. The involved arteries usually become red and thick. Nodules or induration may be felt. Pulsations may be lost.

TABLE 97.—DIFFERENTIAL DIAGNOSIS BETWEEN CRANIAL ARTERITIS AND PERIARTERITIS NODOSA (ESSENTIAL POLYARTERITIS)

| | *Cranial Arteritis* | *Periarteritis Nodosa* |
|---|---|---|
| Age of Patients | Usually 50 years or older | Any age from infancy on |
| Distribution of Lesions | Localized always to the temporal arteries and associated cranial arteries | May involve any artery in the body and usually is generalized. May involve various arteries progressively. May involve veins |
| Eosinophilia | Rare | Occurs in about 20 per cent of cases |
| Prognosis | Good. Never fatal. May lead to blindness | Poor. Usually fatal |

Visual disturbances may appear—photophobia, diplopia and in a number of cases blindness. Constitutional and local symptoms may persist for months or even years.

### Laboratory Findings

There is usually but not always a polymorphonuclear leukocytosis. Eosinophilia is characteristically absent. The sedimentation rate is ordinarily elevated, sometimes tremendously. There may be a mild anemia. The urine is normal, and the results of the Wassermann test are negative. An increased protein content of the cerebrospinal fluid has been reported.

### Diagnosis

The differential diagnosis between cranial arteritis and the disseminated forms of arteritis is usually apparent.

### Treatment

Cases of cranial arteritis may exhibit complete remission of symptoms without treatment. Excision of the involved arteries often but not always relieves the pain. The fever will often continue after the excision. When excision fails to produce relief, deeply situated arteries are probably involved. Roberts and Askey have reported that the periarterial injection of the temporal arteries with procaine hydrochloride (1–2 cc.) brings marked and lasting relief when these arteries alone are involved. Analgesics and sedatives are only partly effective. The use of opiates is to be avoided.

## DISEASES OF THE PERIPHERAL LYMPH VESSELS

The lymph vessels are closed vessels, very similar to the veins in structure. They have valves and an unbroken endothelial lining and are in contact externally with the tissue spaces. Every main blood vessel has an accompanying lymph vessel. Most parts of the body are richly supplied with lymph vessels and in many regions, including the limbs, these are arranged in two systems—the superficial and the deep. The course of each lymph vessel is interrupted by lymph nodes through which the lymph passes on its way toward the systemic circulation. Lymph, the fluid contained in these vessels, contains prothrombin and fibrinogen but is relatively deficient in thromboplastic substance. It clots, therefore, less rapidly than does blood. The pressure of lymph is low and its circulation largely depends on the action of the skeletal muscles aided by the action of the valves in the lymph vessels.

The two common abnormal conditions of the peripheral lymphatics are noninflammatory lymphedema and inflammatory lymphangitis. Both are obstructive conditions. Uncommon abnormalities of the

sistent lymphedema leads to progressive fibrosis, which will not respond to anything less than surgical extirpation. Early lymphedema is not unlike the edema of varicose veins in that there are dilated lymph vessels with incompetent valves and stasis of the circulating fluid. Medical treatment is designed to support the lymph vessels and prevent stasis and the effusion of fluid into the tissue spaces. This is accomplished by compression of the limb with an elastic support.

Before a compression bandage or stocking is fitted to the lymphedematous leg, all possible edema must be removed by putting the patient to bed and elevating the involved limb in a sling. When the size of the limb is reduced satisfactorily, an elastic stocking is fitted to the limb. Non-elastic bandages are useless and elastic bandages are undesirable because they are difficult to apply, tend to slip and curl, and do not exert pressure evenly over the entire leg. Elastic stockings have the disadvantages that they require expert fitting, lose their elasticity after repeated washings, and are expensive. The only criterion is whether the support prevents edema.

The bandage is applied over a lisle stocking—two turns about the foot, two figure-eight turns about the ankle, and so on up to the knee. Experience will teach the patient how to apply the bandage.

The patient puts on the elastic support each morning before getting out of bed and wears it constantly while ambulatory. A midday rest with the leg elevated and the elastic support removed is desirable. Extra elastic supports should be available to permit frequent washing.

*In cases with advanced fibrosis* the wearing of a support may be permanent. In early cases there may be retardation of the lymphedematous process in six months or a year. The rule is to wear a support as long as necessary. Even when the edema has disappeared, a support should be worn during periods of prolonged standing or walking.

The treatment of secondary lymphedema of the arm is based on similar principles. W. T. Foley has devised an elastic half glove and sleeve which has been useful in managing these cases.

*Surgical Treatment.*—Surgical intervention is indicated only in instances of advanced or extensive lymphedema. In milder cases the radical procedures are out of proportion to the deformity produced by the lymphedema and do not assure that the lymphedematous process will not continue.

The most popular procedure has been the Kondoleon operation, in which the skin of three-quarters of the circumference of the extremity is undermined and the fascial sheath of the muscle is completely removed. This permits the superficial lymph to drain through the muscular lymphatics. A recent technique involves the subcutaneous insertion of threads to encourage the drainage of lymph around sites of obstruction.

## LYMPHANGITIS

### (Inflammatory Lymphedema)

Lymphedema of inflammatory origin is the result of single or recurrent attacks of acute cellulitis and lymphangitis. Primary lymphangitis, the more common form, occurs abruptly as a result of bacterial infection, ordinarily streptococcic, although the portal of entry is usually obscure. Secondary lymphangitis arises from local injuries or infections, trichophytosis, systemic infections or infestations, and filariasis. The following classification is based on etiological considerations.

Etiological Classification of Lymphangitis (Inflammatory Lymphedema)

1. Primary lymphangitis (cause unknown)
2. Secondary lymphangitis due to
   a. Filariasis
   b. Trichophytosis
   c. Local tissue injury or inflammation (lacerations, bites, burns, furuncles, other local infections, chemical, non-bacterial)
3. Erysipelas

### Cellulitis and Lymphangitis

The acute attack of cellulitis and lymphangitis is ushered in by a shaking chill, sometimes preceded by a brief period of discomfort in the involved extremity or its proximal lymph nodes. The patient's

to play an important part in the production of the condition

*Congenital Lymphedema* —Congenital lymphedema may be non hereditary or hereditary (Milroy's disease) In simple congenital lymphedema there is a diffuse swelling involving part or all of a single extremity at birth As growth occurs, the size of the involved extremity continues to be greater than that of the uninvolved limb The swelling is firm, pits on pressure and is reduced by prolonged elevation There is no pain nor do ulceration or inflammation occur The length of the extremity is not greater than that of the opposite limb nor is the temperature of the limb elevated above that of the companion limb as in congenital arteriovenous fistula

*Secondary Lymphedema* —This type of lymphedema arises from occlusion of lymph vessels by metastatic malignancies or lymphoblastomas, from obliteration of the lymph channels by surgical removal of the lymph nodes, or from post irradiation therapy There may be intercurrent attacks of lymphangitis or cellulitis

Lymphedema secondary to filariasis is common in areas where this infestation is endemic but rare in the United States Filariasis is discussed in the section on Nematode infections (Chapter 8)

TABLE 58 —THE DIFFERENTIAL DIAGNOSIS OF LYMPHEDEMA

| *Condition* | *Differential Features* |
|---|---|
| | I SYSTEMIC DISEASES |
| Congestive Heart Failure Myxedema Nephritis Nephrosis Hypoproteinemia | There is no difficulty in distinguishing unilateral lymphedema from the bilateral edema of systemic disease Careful and complete examination is necessary when lymphedema is bilateral |
| | II VASCULAR DISEASES OF THE LIMB |
| Arteriovenous Fistula | In *A–V* fistula there is enlargement of the limb increased pressure in and dilatation of the regional veins venous oxygen content approaching that of the arteries *If A–V fistula is congenital or acquired early in life* the limb is increased in length as well as in circumference Limb is warmer than its opposite |
| Chronic Venous Insufficiency | |
| Early | Differentiation is often difficult Venous insufficiency may be apparent from mode of onset rapidity of onset and progress amount of distress to the patient and dilatation of superficial veins The two conditions exist together rarely |
| Late | Edema of venous insufficiency is softer and is accompanied by dermatitis stasis ulcers and superficial varices Lymphedema does not lead to eczematoid dermatitis ulceration or superficial varicosities |
| | III OTHER CONDITIONS IN THE LIMB |
| Lipodystrophy | Lipodystrophy is bilateral and is usually associated with generalized obesity or obesity around the waist and hips It does not extend although it may become more pronounced There is less pitting in lipodystrophy Lipodystrophy is never accompanied by cellulitis and lymphangitis Bed rest and elevation of the limb have little influence on lipodystrophy |
| Malignant and Benign Tumors | These are unilateral Edema is localized or regionalized Lymphosarcoma produces extensive edema of lymphatic origin but the regional lymph nodes are enlarged Roentgen examination and biopsy will assist in the diagnosis |
| *Angioneurotic Edema* | Characteristically cyclic in character |
| Neurofibromatosis | Nodular enlargements and neurofibromata elsewhere |

TREATMENT

*Medical Treatment* —Treatment of lymphedema must be instituted at once Per

Wright I S Vascular Diseases in Clinical Practice Yearbook Publishers Chicago 1948

REVIEWS AND ORIGINAL ARTICLES

*Hypertension*

Gressel G C Shore F O Saslow G Dubois P H and Schroeder H A Arterial Hypertension J A M A 1949 *140* 265

Keith N M Wagener H P and Kernohan J W The Syndrome of Malignant Hypertension Arch Int Med 1928 *41* 141

Roth G M and Kvale W F Pharmacologic Tests as an Aid in Diagnosis of Pheochromocytoma Med Concepts Cardiovas Dis May 1949

Shorr E Participation of Hepatorenal Vasotropic Factors in Experimental Renal Hypertension Am J Med 1948 4 120

Smith H W Goldring W and Chasis H Rôle of the Kidney in the Genesis of Hypertension Bull N Y Acad Med 1943 *19* 449

Wagener H P and Keith N M Diffuse Arteriolar Disease with Hypertension and the Associated Retinal Lesions Medicine 1939 *18* 317

*Hypotension*

Corcoran A C Browning J S and Page I H Renal Hemodynamics in Orthostatic Hypotension Effect of Angiotonin and Head up Bed J A M A 1942 *119* 793

MacLean A R and Allen E V Orthostatic Hypotension J A M A 1940 *115* 2162

Stead E A Jr and Ebert R V Postural Hypotension Disease of Sympathetic Nervous System Ann Int Med 1941 *117* 546

*Peripheral Vascular Diseases*

*Raynaud s Phenomenon*

Allen E V and Brown G E Raynaud s Disease A Critical Review of Minimal Requisites for Diagnosis Am J Med Sci *1932 183* 187

Hyndman O R and Wolkin J Raynaud s Disease A Review of Its Mechanism with Evidence that It is Primarily a Vascular Disease Am Heart J 1942 *23* 535

*Erythermalgia*

Smith L A and Allen E V Erythermalgia (Erythromelalgia) of the Extremities Am Heart J 1938 *16* 175

Mufson I Clinical Observations in Erythromelalgia and a Method for Its Symptomatic Relief Am Heart J 1937 *13* 483

*Syndromes Due to Heat and Cold*

Blackwood W Studies in Pathology of Human Immersion Foot Brit J Surg 1944 *29* 329

Horton B T Brown G E and Roth G M Hypersensitiveness to Cold with Local and Systemic Manifestations of a Histamine-like Character Its Amenability to Treatment J A M A 1936 *107* 1263

Lange K and Boyd L J The Functional Pathology of Experimental Frostbite and the Prevention of Subsequent Gangrene Surg Gynec and Obstet 1945 *77* 561

*McGovern T and Wright I S Pernio a Vascular Disease* Am Heart J 1941 *22* 583

*Neurovascular Syndromes of the Shoulder Girdle*

Wright I S Neurovascular Syndrome Produced by Hyperabduction of the Arms Immediate Changes Produced in 150 Normal Controls and *Effects on Some Persons of Prolonged* Hyperabduction of Arms as in Sleeping and in Certain Occupations Am J Heart 1945 *29* 1

*Arteriosclerosis*

Cowdry E V Arteriosclerosis Macmillan Company New York 1933

Dock W The Causes of Arteriosclerosis Bull N Y Acad Med 1950 *26* 182

Dry T J and Hines E A Jr The Rôle of Diabetes in the Development of Degenerative Vascular Disease with Special Reference to the Incidence of Retinitis and Peripheral Neuritis Ann Int Med 1941 *14* 1893

Gofman J W *et al* Blood Lipids and Human Atherosclerosis Circulation 1950 *II* 161

Leary T Atherosclerosis Etiology Criticisms of Experimental Evidence Pointing to Cholesterol Arch Path 1936 *21* 459

Weinhouse S and Hirsch E F Chemistry of Atherosclerosis I Lipid and Calcium Content of the Intima and of the Media of the *Aorta with and without Atherosclerosis* Arch Path 1940 *29* 31

Editorial Experimental Atherosclerosis J A M A 1950 *142* 262

*Arteriosclerosis Obliterans*

Hines E A Jr and Barker N W Arteriosclerosis Obliterans *A Clinical and Pathologic Study* Am J Med Sci 1940 *200* 717

Wright I S The Treatment of Arteriosclerosis Obliterans Social Significance and Ultimate Objective J A M A 1940 *115* 893

———Conservative Treatment of Occlusive Arterial Disease Arch Surg 1940 *40* 163

*Thromboangiitis Obliterans*

Allen E V Thromboangiitis obliterans Bull N Y Acad Med 1942 *18* 167

Wright I S and Moffat D The Effects of Tobacco on the Peripheral Vascular System Am Heart J 1934 *12* 318

*Acute Arterial Occlusion*

Freeman N E Leeds F H and Gardner R E Arterectomy in the Treatment of Intractable Pain Following Recovery from Acute Arterial Occlusion Am Heart J 1949 *38* 329

temperature rises rapidly to 101 to 105° F (38 3 to 40 5° C ) An area of rubor appears at the site of the inflammation and spreads rapidly The involved area is hot tender, and swollen The regional lymph nodes become swollen and tender The temperature remains elevated for some hours and chills recur at intervals There is marked malaise and there may be nausea and vomiting The ordinary attack subsides in a few days, but the recession of the signs of acute inflammation may be followed by a persistent degree of edema When attacks are recurrent, each attack leaves a greater degree of residual edema There may be some permanent discoloration of the skin In all types of inflammatory lymphedema, the attacks of acute lymphangitis are accompanied by thrombosis of the lymph channels This thrombosis produces the obstruction and stasis which contributes to the progressive edema formation

## Treatment

Acute lymphangitis is always a serious condition Its prevention is important but, in many cases there are no premonitory signs Active treatment includes putting the patient to bed elevating the affected limb, and applying moist hot packs from toe to groin when the leg is involved and from the fingers to the axilla when the arm is involved Antibiotics should be administered freely A search should be made for a primary portal of entry, which may be a superficial abrasion, an interdigital fissure or a chronic leg ulcer Acute lymphangitis is particularly hazardous when it involves a limb rendered relatively ischemic by obliterative vascular disease

Local treatment includes the elimination of factors which favor infection eradication of infected epidermophytosis removal of eschars over infected wounds or ulcers, incision and drainage of abscesses Recurrent lymphangitis complicating another peripheral vascular condition will usually fail to respond until the underlying disease is controlled

## TEXTS AND MONOGRAPHS

### *Hypertension*

Braun Menendez E Fasciolo J C Leloir L F Munoz J M and Taquini A C (Translated by Lewis Dexter) Renal Hypertension Charles C Thomas Springfield 1946

Goldblatt H The Renal Origin of Hypertension Charles C Thomas Springfield 1948

Goldring W and Chasis H Hypertension and Hypertensive Disease, The Commonwealth Fund New York 1944

Grimson K S The Surgical Treatment of Hypertension Chapter 4 in Advances in Internal Medicine, Vol 2 Interscience Press New York 1947

Page I H H and Corcoran A C Arterial Hypertension Its Diagnosis and Treatment The Year Book Publishers Chicago 1945

Trueta, J Barclay A E Daniel P M, Franklin K J and Prichard M M L Studies of the Renal Circulation Blackwell Scientific Publications Oxford 1947

White P D Hypertensive Heart Disease Essential Hypertension Hypotension Chapter 18 in Heart Disease ed 3 Macmillan Co New York 1945

———Hypertension in Yearbooks of Medicine Yearbook Publishers Chicago 1937–1949

———Nomenclature and Criteria for Diagnosis of Diseases of the Heart ed 4 New York Heart Assoc New York 1945

### *The Peripheral Vascular Diseases*

Abrahamson D I Vascular Responses in the Extremities of Man in Health and Disease Univ Chicago Press Chicago 1944

Allen E V Barker N W and Hines E A, Jr Peripheral Vascular Diseases W B Saunders Philadelphia 1946

Barrow D W The Clinical Management of Varicose Veins Hoeber New York 1949

Burch G A Primer of Venous Pressure Lea & Febiger Philadelphia 1950

Holman E Arteriovenous Aneurysm Abnormal Communications Between the Arterial and Venous Circulations Macmillan New York 1937

Jorpes E Heparin in the Treatment of Thrombosis Oxford London ed 2 1946

Kramer D W Peripheral Vascular Diseases F A Davis Co Philadelphia 1948

Lewis T Exercises in Human Physiology Macmillan London 1945

Marple C D and Wright I S Thromboembolic Conditions and Their Treatment with Anticoagulants Charles C Thomas Springfield Ill 1950

Pratt G Surgical Management of Vascular Diseases Lea & Febiger Philadelphia 1949

Quiring D P Collateral Circulation Lea & Febiger Philadelphia 1949

WRIGHT I S Vascular Diseases in Clinical Practice Yearbook Publishers Chicago 1948

## REVIEWS AND ORIGINAL ARTICLES

### *Hypertension*

GRESSEL, G C SHORE F O SASLOW G DUBOIS P H and SCHROEDER H A Arterial Hypertension J A M A 1949 *140* 265

KEITH N M WAGENER H P and KERNOHAN J W The Syndrome of Malignant Hypertension Arch Int Med 1928 *41* 141

ROTH G M and KVALE W F Pharmacologic Tests as an Aid in Diagnosis of Pheochromocytoma Med Concepts Cardiovas Di May 1949

SHORR E Participation of Hepatorenal Vasotropic Factors in Experimental Renal Hypertension Am J Med 1948 4 120

SMITH H W GOLDRING W and CHASIS H Rôle of the Kidney in the Genesis of Hypertension Bull N Y Acad Med 1943 *19* 449

WAGENER H P and KEITH N M Diffuse Arteriolar Disease with Hypertension and the Associated Retinal Lesions Medicine 1939 *18* 317

### *Hypotension*

CORCORAN A C BROWNING J S and PAGE I H Renal Hemodynamics in Orthostatic Hypotension Effect of Angiotonin and Head up Bed J A M A 1942 *119* 793

MACLEAN A R and ALLEN E V Orthostatic Hypotension J A M A 1940 *115* 2162

STEAD E A JR and EBERT R V Postural Hypotension Disease of Sympathetic Nervous System Ann Int Med 1941 *117* 546

### *Peripheral Vascular Diseases*

#### *Raynaud's Phenomenon*

ALLEN E V and BROWN G E Raynaud's Disease A Critical Review of Minimal Requisites for Diagnosis Am J Med Sci 1932 *183* 187

HYNDMAN O R and WOLKIN J Raynaud's Disease A Review of Its Mechanism with Evidence that It is Primarily a Vascular Disease Am Heart J 1942 *23* 535

#### *Erythermalgia*

SMITH L A and ALLEN E V Erythermalgia (Erythromelalgia) of the Extremities Am Heart J 1938 *16* 175

MUFSON I Clinical Observations in Erythromelalgia and a Method for Its Symptomatic Relief Am Heart J 1937 *13* 483

#### *Syndromes Due to Heat and Cold*

BLACKWOOD W Studies in Pathology of Human Immersion Foot Brit J Surg 1944 *29* 329

HORTON B T BROWN G E and ROTH G M Hypersensitiveness to Cold with Local and Systemic Manifestations of a Histamine-like Character Its Amenability to Treatment J A M A 1936 *107* 1263

LANGE K and BOYD L J The Functional Pathology of Experimental Frostbite and the Prevention of Subsequent Gangrene Surg Gynec and Obstet 1945 77 561

MCGOVERN T and WRIGHT I S Pernio a Vascular Disease Am Heart J 1941 *22* 583

#### *Neurovascular Syndromes of the Shoulder Girdle*

WRIGHT I S Neurovascular Syndrome Produced by Hyperabduction of the Arms Immediate Changes Produced in 150 Normal Controls and Effects on Some Persons of Prolonged Hyperabduction of Arms as in Sleeping and in Certain Occupations Am J Heart 1945 *29* 1

#### *Arteriosclerosis*

COWDRY E V Arteriosclerosis Macmillan Company New York 1933

DOCK W The Causes of Arteriosclerosis Bull N Y Acad Med 1950 *26* 182

DRY T J and HINES E A JR The Rôle of Diabetes in the Development of Degenerative Vascular Disease with Special Reference to the Incidence of Retinitis and Peripheral Neuritis Ann Int Med 1941 *14* 1893

GOFMAN J W *et al* Blood Lipids and Human Atherosclerosis Circulation 1950 *II* 161

LEARY T Atherosclerosis Etiology Criticisms of Experimental Evidence Pointing to Cholesterol Arch Path 1936 *21* 459

WEINHOUSE S and HIRSCH E F Chemistry of Atherosclerosis I Lipid and Calcium Content of the Intima and of the Media of the Aorta with and without Atherosclerosis Arch Path 1940 *29* 31

Editorial Experimental Atherosclerosis J A M A 1950 *142* 262

#### *Arteriosclerosis Obliterans*

HINES E A JR and BARKER N W Arteriosclerosis Obliterans A Clinical and Pathologic Study Am J Med Sci 1940 *200* 717

WRIGHT I S The Treatment of Arteriosclerosis Obliterans Social Significance and Ultimate Objective J A M A 1940 *115* 893

——— Conservative Treatment of Occlusive Arterial Disease Arch Surg 1940 *40* 163

#### *Thromboangiitis Obliterans*

ALLEN E V Thromboangiitis obliterans Bull N Y Acad Med 1942 *18* 167

WRIGHT I S and MOFFAT D The Effects of Tobacco on the Peripheral Vascular System Am Heart J 1934 *10* 318

#### *Acute Arterial Occlusion*

FREEMAN N E LEEDS F H and GARDNER R E Arterectomy in the Treatment of Intractable Pain Following Recovery from Acute Arterial Occlusion Am Heart J 1949 *38* 329

SALAND G Acute Occlusions of the Peripheral Arteries Clinical Analysis and Treatment Ann Int Med 1941 *14* 2027

WRIGHT I S and FOLEY W T Use of Anticoagulants in Treatment of Heart Disease Am J Med 1947 *3* 718

*Temporal Arteritis*

HORTON B T Arteritis of the Temporal Vessels A Previously Undescribed Form Arch Int Med 1934 *53* 400

SCHAEFER C L and SANDERS C E Temporal Arteritis Am Heart J 1942 *24* 410

*Aneurysm*

GLENDY R L CASTLEMAN B and WHITE P D Dissecting Aneurysm of the Aorta A Clinical and Anatomical Analysis of Nineteen Cases (Thirteen Acute) with Notes on the Differential Diagnosis Am Heart J 1937 *12* 129

MILLS J H and HORTON B T Clinical Aspects of Aneurysm Arch Int Med 1938 *62* 949

MOTE C D and CARR J L Dissecting Aneurysm of the Aorta Am Heart J 1942 *24* 69

PEMBERTON J DEJ and MAHORNER H R Aneurysms Associated with Thromboangiitis Obliterans Surg Clin North Am 1932 *12* 893

*Arteriovenous Fistula*

KENNEDY J A and BURWELL C S Measurements of the Circulation in a Patient with Multiple Arteriovenous Connections Am Heart J 1944 *28* 133

LEWIS T The Adjustment of Blood Flow to the Affected Limb in Arteriovenous Fistula Clin Sci 1940 *4*, 277

*Coarctation of the Aorta*

BAHNSON H T COOLEY R N and SLOAN R D Coarctation of the Aorta at Unusual Sites Am Heart J 1949 *38* 905

*Diseases of the Veins*

*Thrombophlebitis*

BARKER N W NYGAARD K K WALTERS W and PRIESTLEY J T A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism Proc Staff Meet Mayo Clinic 1940 *15* 769 *ibid* 1941 *16* 1 17 33

COSGRIFF S W CROSS R J and HABIF D V The Management of Venous Thrombosis and Pulmonary Embolism Surg Clin North Am 1948 *28* 324

McCARTNEY E T and LEWIS A S Pulmonary Embolism Arising from Great Saphenous Vein Brit J Surg 1949 *37* 45

WRIGHT, I S Practical Considerations in the Conservative Treatment of Thrombophlebitis N Y State J Med 1946 *46* 1819

*Varicose Veins*

EDWARDS J E and EDWARDS L A The Saphenous Valves in Varicose Veins Am Heart J 1940 *19* 338

LARSON R A and SMITH F L Varicose Veins Evaluation of Observations on 491 Cases Proc Staff Meet Mayo Clinic 1943 *18* 400

SZILAGYI D E and ALSOP J F Early and Late Sequellæ of Therapeutic Vein Ligation for Thrombosis of Veins of Lower Limbs Arch Surg 1949, *59* 633

WARREN R WHITE E A and BELCHER C D Venous Pressures in Saphenous System in Normal Varicose and Post phlebitis Extremities Alterations Following Femoral Vein Ligation Surg 1949 *26* 435

*Venous Insufficiency*

HEYERDALE W and CANNON E E Neurodermatitis Associated with Incompetent Greater Saphenous Veins Report of Case Arch Dermat & Syph 1941 *44* 52

MURRAY C K and SHAAR C M Red Blood Cell Paste in Treatment of Ulcers and Chronically Infected Wounds J A M A 1944 *125* 779

PRATT G H Sympathectomy in Treatment of Certain Vascular Lesions with Report on Its Use in *Post thrombotic Syndrome* N Y State J Med 1949 *49* 2161

*Diseases of the Lymph Vessels*

*Lymphedema*

ALLEN E V Lymphedema of the Extremities Classification Etiology and Differential Diagnosis A Study of 300 Cases Arch Int Med 1934 *54* 606

HOMANS J DRINKER C K and FIELD M E Elephantiasis and the Clinical Implications of Its Experimental Reproduction in Animals Ann Surg 1934 *100* 812

PRATT G H and WRIGHT I S Surgical Treatment of Chronic Lymphedema (Elephantiasis) Surg Gynec & Obstet 1941 *72* 244

*Lymphangitis*

OCHSNER A LONGACRE A B and MURRAY S D Progressive Lymphedema Associated with Recurrent Erysipeloid Infections Surg 1940 *8* 383

# Chapter 25

# Diseases of the Blood

By CYRUS C. STURGIS, M.D.

## INTRODUCTION

The circulating blood is a suspension of erythrocytes, leukocytes and platelets in liquid plasma. The main function of the red blood cells by virtue of their hemoglobin is the transportation of oxygen from the lungs to the tissues; that of the leukocytes chiefly the defense of the body against infection, and that of the platelets the coagulation of blood.

The normal blood values of an adult male weighing 70 kilograms are as follows:

| | |
|---|---|
| Total blood volume (80 c.c. per kilo) | 5600 c.c. |
| Average red blood cells per cubic millimeter | 5.4 million |
| Total number of red blood cells in body | 3 trillion |
| Average duration of life of red blood cell | 120 days |
| Number of red blood cells replaced daily in body | 25 billion |
| Hemoglobin content of blood per 100 cc. | 15.6 grams |
| Total hemoglobin in body | 859 grams |
| Amount of iron in hemoglobin | 0.334 per cent |
| Amount of iron in total hemoglobin of circulating blood | 2.877 grams |

### Normal Hematologic Standards and Some Diagnostic Measures Employed in Examination of the Blood

Important data on the volume of the red blood cells and their hemoglobin content are obtained by calculations based on the red blood cell count, the hemoglobin determination, and the estimation of the volume of packed red blood cells by means of the hematocrit.

The more important values are:

(1) Mean Corpuscular Volume (cubic microns)

$$\frac{\text{Vol. Packed Red Blood Cells, c.c. per 1000 c.c.}}{\text{R.B.C. millions per cu. mm.}}$$

(2) Mean Corpuscular Hemoglobin Concentration (%) (M.C.H.C.)

$$\frac{\text{Hb. Grams per 100 c.c.} \times 100}{\text{Vol. Packed Red Blood Cells, c.c. per 100 c.c.}}$$

(3) Mean Corpuscular Hemoglobin (Micromicrograms) (M.C.H.)

$$\frac{\text{Hb. in Grams per 1000 c.c.}}{\text{R.B.C. Millions per cu. mm.}}$$

(4) *Color Index*

$$\frac{\text{Hb. in Grams per 100 c.c.} \times 6.4}{\text{R.B.C. in millions per cu. mm.} \times 20}$$

The following table shows the normal hematological standards collected by Dr. Frank H. Bethell and used at the Simpson Memorial Institute of the University of Michigan.

TABLE 59

| | Men | | Women | |
|---|---|---|---|---|
| | *Range** | *Average* | *Range** | *Average* |
| Number of red blood cells per cu mm | 4 70– 6 00 | 5 35 | 4 13– 5 21 | 4 67 |
| Hemoglobin grams per 100 c c | 13 39–17 63 | 15 51 | 12 17–15 01 | 13 59 |
| Packed Cell Volume (hematocrit) per cent | 41 36–52 88 | 47 12 | 37 66–45 44 | 41 60 |
| Mean Corpuscular Hemoglobin micromicrograms | 26 08–32 00 | 29 04 | 26 34–32 02 | 29 13 |
| Mean Corpuscular Hemoglobin Concentration, per cent | 30 21–35 62 | 32 92 | 30 12–35 08 | 32 60 |
| Mean Corpuscular Volume, cubic microns | 81 26–95 26 | 88 26 | 82 17–96 85 | 89 51 |
| Color Index | 0 90– 1 10 | 1 00 | 0 90– 1 10 | 1 00 |
| Volume Index | 0 91– 1 07 | 1 00 | 0 92– 1 09 | 1 00 |
| Saturation Index | 0 92– 1 09 | 1 00 | 0 92– 1 07 | 1 00 |

* The ranges include 95 per cent of all observations on normal subjects and are derived from data which have been shown to be statistically significant

TABLE 60

| *Type of Anemia* | *M C V cu microns* | *M C Hb C per cent* | *Color Index* |
|---|---|---|---|
| Macrocytic normochromic | 96–160 | 30–35 | 1 0 |
| Normocytic normochromic | 82–96 | 30–35 | 1 0 |
| Microcytic hypochromic | 50–92 | 21–29 | 0 5–0 9 |

By utilizing the mean corpuscular volume and the mean corpuscular hemoglobin concentration it is possible to recognize the different types of anemia based on the volume of the red blood cells and their hemoglobin content The three most important with one example of each are as follows (1) macrocytic normochromic anemia (Addisonian pernicious anemia) (2) normocytic normochromic anemia (the anemia of infection), (3) microcytic hypochromic (iron deficiency anemia)

Table 60 gives the average findings for each of the three different types of anemia

## WHITE BLOOD CELLS

These cells numbering from 5000 to 10,000 per cubic millimeter in the peripheral blood have as their chief function the defense against infection in the body When their number falls below 5000 per cubic millimeter a *leukopenia* is said to be present when the number is above 10,000 per cubic millimeter there is a *leukocytosis* These cells are characterized by (1) a relatively short life, 2 to 3 days, (2) the power of motility which permits at least some of them to engulf microorganisms and to migrate from the blood stream into the tissues and (3) the presence of digestive enzymes The percentages of the various types of leukocytes are as follows Neutrophils, band 3–6%, lobed 55–57% total 58–67%, eosinophils 1–3% basophils 0–1% lymphocytes 20–30% monocytes 5–9%

The conditions commonly associated with a neutrophilia are (1) acute infections especially with staphylococci and streptococci (2) intoxications as uremia and acidosis (3) hemolysis (4) severe acute hemorrhage (following operations especially those involving the abdominal cavity) malignancy, and myelogenous leukemia

Causes of a leukopenia are (1) infections especially those due to a virus such as influenza and measles (2) an overwhelming infection of any type (3) diseases of the blood forming organs as pernicious anemia

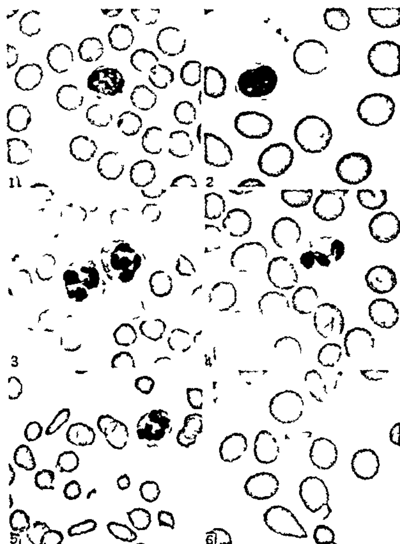



Fig 181 —Variation in the shape and size of the erythrocyte (photomicrographs × 1100) 1 Normal red cells Note the uniform diameter and central depression 2 Macrocytes in pernicious anemia The cells are large and filled with hemoglobin 3 Microcytes in hypochromic anemia The cells are quite small and very pale due to the low hemoglobin content 4 The flattened cell of chronic obstructive jaundice The volume of the cells is normal but the diameter is uniformly increased so the thickness is less than normal 5 The red cells in idiopathic hypochromic anemia These show marked microcytosis hypochromia and anisocytosis The elongated cells are quite characteristic of this condition 6 Poikilocytosis in pernicious anemia The oval and pear shaped cells are commonly seen in pernicious anemia (Haden s Principles of Hematology)

aplastic anemia acute and subleukemic leukemias and primary splenic neutropenia (4) agranulocytosis usually due to drugs and (5) Banti s Felty s and Gaucher s disease

A lymphocytosis may be present in infancy and childhood and in (1) certain infections as pertussis rubella infectious lymphocytosis and infectious mononucleosis (2) lymphatic reactions to infectious disease in childhood (3) tuberculosis with good resistance (4) exophthalmic goiter and (5) lymphatic leukemia A lymphopenia may be seen in (1) advanced Hodgkin s disease (2) excessive irradiation (3) agranulocytosis (4) leukemia other than lymphatic (5) tuberculosis with poor resistance (6) infections with increase in neutrophils

A monocytosis may be observed in (1) chronic pyogenic infections (2) protozoal infections as malaria (3) subacute bacterial endocarditis (4) typhus and Rocky Mountain spotted fever, (5) in some cases of Hodgkin s disease (6) tuberculosis with poor resistance (7) monocytic leukemia

An eosinophilia may be associated with the following conditions (1) parasitic infestations (2) allergic conditions (3) skin diseases (4) disseminated vascular disease (5) pernicious anemia treated with liver diet

A basophilia may be seen (1) in association with an increase in the eosinophils and (2) in chronic myelogenous leukemia

## Incidence of Blood Diseases

Evidence accumulated in the past decade indicates that anemia is perhaps more common than previously suspected For example in about 25,000 routine admissions of patients over 14 years of age in the in patient and out patient departments of the University of Michigan Hospital an anemia of clinical significance was found in one out of every 8 persons (12 per cent) Of these the most frequently observed (41 per cent) was a normocytic normochromic type usually due to a chronic infection and less commonly to chronic nephritis Next in frequency (39 per cent) was a microcytic hypochromic anemia resulting from an iron deficiency which is usually secondary to chronic hemorrhage The remaining group included patients with myelophthisic anemia in association with various conditions as leukemia Hodgkin s disease and different types of cancer the macrocytic anemias such as pernicious anemia refractory anemias and the hemolytic anemias

It is of interest to note that in a routine study of a group of normal pregnant women it was found that 54 per cent had an anemia more severe than the physiologic anemia of pregnancy, and of these the largest proportion had an anemia of the iron deficiency type In recent years, certain anemias as for example the sickle cell variety have been recognized as occurring with greater frequency among Negroes and Mediterranean anemia occurring usually in persons of Greek or Italian ancestry, is not so rare in the United States as previously supposed

There is convincing evidence to show that leukemia is observed more often than it has been This is due in part to better diagnostic methods As the increase is in all age groups however, it cannot be attributed to the fact that more persons live longer than middle age Pernicious anemia is observed more commonly now than it was fifty years ago partly because diagnostic methods are more accurate and partly because more persons live to the age at which the disease most commonly occurs

## The Mechanisms of the Production of the Anemias

An anemia may be defined as a diminution in the concentration of hemoglobin or erythrocytes or both below the standards accepted as normal for age and sex Such a condition may arise as a result of deficient formation or increased destruction of blood or a combination of the two In health the number of formed elements of the peripheral blood the erythrocytes the leukocytes and the platelets are maintained at a constant level with great exactness In the case of the erythrocytes and probably also the leukocytes and platelets this is possible because in any given period of time just as many red blood cells are delivered from the bone marrow to the circulation as are destroyed

If blood is lost by hemorrhage failure of the marrow to produce red blood cells at a normal rate or abnormal destruction of red blood cells the delicate balance which maintains the blood at a constant level is upset and an anemia results Aplastic anemia with actual destruction of the bone marrow as the result of poisoning (as for example with benzol) is an excellent example of an anemia due to decreased blood formation An anemia which probably results solely from increased destruction of red blood cells is chronic hemolytic anemia of the congenital type In this condition it is possible to demonstrate that the red blood cells are more fragile than normal this explains at least in part why they are so readily destroyed

A great majority of anemias arise primarily on account of deficient blood formation due either to an inability to synthesize hemoglobin normally or to a slowing up of the rate of red blood cell maturation. *Hemoglobin* is formed in the body from heme which is derived from glycine and acetic acid acting in combination with globin and iron. This process occurs in the red blood cells of the bone marrow, chiefly at the normoblast and reticulocyte stages over a period of several days. Ordinarily there is no lack of globin or heme in the body, but a common cause of anemia is a deficiency of iron, without which hemoglobin cannot be formed. With lack of this metal there is a deficiency of hemoglobin and a microcytic hypochromic anemia results. The inability to synthesize hemoglobin normally probably also accounts for the development of another common type of anemia, namely, the anemia *of infection*. Although all the factors which control the rate of formation of the erythrocytes are not known, it is recognized *that pteroylglutamic acid (folic acid) and the* recently discovered vitamin $B_{12}$ play important roles in the regulation of this process. For example, in nutritional anemia there is probably a deficiency of folic acid and in Addisonian pernicious anemia one of vitamin $B_{12}$, a deficiency that results in a retarded rate of development of the red blood cells in the bone marrow. Consequently, as blood destruction proceeds at a normal (or perhaps an accelerated) rate, an anemia of the macrocytic type must result. Decreased blood production is shown by an absence or sparsity of immature forms of red blood cells such as reticulocytes, nucleated erythrocytes, and cells showing polychromatophilia.

Anemia due to increased destruction of red blood cells (hemolytic anemia) is less common than anemia due to decreased blood formation. Evidences of increased destruction are hyperbilirubinemia, fever and frequently a palpable spleen. With an increase in the amount of bilirubin in the plasma there develops an icteric tint in the skin and conjunctivae which is apparent in the various hemolytic anemias. As bilirubin is derived from hemoglobin, it has been assumed that the amount present in the plasma is a rough index of the extent of *blood destruction. While this is undoubtedly* true in some instances, in certain anemias such as pernicious anemia it must be admitted that an excess of bilirubin in the plasma may mean nothing more than a failure to use all of this available material in the formation of red blood cells.

It is interesting to note that all three formed elements of the blood are subject to alterations in numbers, there being either an increase or decrease in various diseases. For example, the red cells are diminished in the anemias and increased in polycythemia. The white blood cells are increased in the leukemias and decreased in agranulocytic angina. The platelets are diminished in some types of purpura and increased following *hemorrhage, after splenectomy,* and sometimes in the chronic leukemias. In most diseases of the blood, although the pre*dominating change is in the number of any* one of the three formed elements, there is almost always an associated change in the *other two.*

## SYMPTOMS AND SIGNS IN DISEASES OF THE BLOOD

In diseases of the blood there are symptoms and signs which are due to various changes, such as enlarged lymph glands, splenomegaly and hepatomegaly, and to the development of the commonly associated anemia of varying degree. The latter is often the more important. Symptoms due to the anemia may result from (1) rapid loss of blood, a loss that manifests itself chiefly by evidences of shock; (2) rapid destruction of blood, such a condition as is seen in acute hemolytic crises (common causes of jaundice and fever in the hemolytic anemias); and (3) the anemia *per se*, a condition that produces manifestations in direct proportion to the level of the hemoglobin of the circulating blood.

When the hemoglobin falls to the vicinity of 11 grams (70 per cent), the symptoms of anemia usually become apparent, and as the hemoglobin falls they become more severe. Evidences of an anemia are pallor, weakness, ease of fatigue, dyspnea, palpitation, vertigo, fainting attacks and sometimes edema of

the ankles *Pallor* as observed in the face is not always indicative of anemia, for the color of a person s skin is not entirely dependent on the hemoglobin level in the blood It is also concerned with the distribution and size of the skin capillaries, natural pigmentation sunburn, artificial coloring and excessive fatigue Recently developing and persistent pallor, however, is likely to be indicative of the presence of an anemia Usually the anemia can be detected more accurately by observing the mucous membranes or the palms of the hands

*Dyspnea* and *palpitation* on exertion are almost invariably associated with anemia, although rarely do these manifestations appear when the patient is at rest These complaints are due to the diminished capacity of the blood to carry oxygen to the tissues When exertion demands an increase in oxygen, the amount of air breathed and the circulatory rate are increased with the consequent production of these symptoms

*Weakness* and *ease of fatigue* are the most constant complaints associated with anemia and may be of such extreme grade as to confine the patient to bed These complaints are associated with the inability of the cardiovascular apparatus to deliver sufficient oxygen to the tissues for the necessary combustion incident to muscular exertion

*Edema of the ankles* is not infrequently observed in the severe anemias but its cause is not always apparent That it is closely associated with the anemia is suggested by its disappearance when the blood returns to normal although some time may elapse before this occurs In some instances it undoubtedly results from a poor appetite and a suboptimal intake of protein with the consequent development of low plasma proteins and an associated decreased osmotic pressure, in other patients it may be due to an associated myocardial weakness or to changes in the blood capillary walls following nutritional disturbances which make them more permeable to fluid

*Vertigo* and *faintness* are considered to be due to an anoxia of the brain

IMPORTANCE OF AN ACCURATE DIAGNOSIS

An accurate diagnosis is absolutely essential in the management of various blood diseases If the anemia is detected by demonstration of a low hemoglobin, and a combination type of therapy instituted in the hope that the patient will improve, some good may be accomplished but this method of therapy invites failure and does not provide an intelligent basis for establishing a prognosis A thorough history and physical examination must be done, along with a complete blood study, including an accurate hematocrit determination, to provide a basis for estimating the cell volume and hemoglobin content Additional studies as roentgen ray examinations, biopsy and sternal puncture may be necessary before the actual diagnosis is established

REFERENCES

FOWLER W M Hematology 2d ed New York Paul B Hoeber, Inc 1949
Handbook of Hematology Edited by Hal Downey New York Paul B Hoeber Inc Medical Book Department of Harper and Brothers 1938
KRACKE ROY R Diseases of the Blood and Atlas of Hematology 2d ed Philadelphia J B Lippincott Company 1941
OSGOOD EDWIN E Atlas of Hematology San Francisco J W Stacey Inc 1937
STURGIS C C Hematology Springfield Ill Charles C Thomas 1948
WHITBY L E H and BRITTON C J C Disorders of the Blood 6th ed London J & A Churchill Ltd
WINTROBE MAXWELL I Clinical Hematology 3d ed Philadelphia Lea & Febiger 1951

## IRON DEFICIENCY (MICROCYTIC HYPOCHROMIC) ANEMIA

By CYRUS C STURGIS, M D

*Definition* —An iron deficiency anemia is a commonly occurring microcytic hypochromic variety which results from an inadequate supply of available iron in the body for the formation of a normal amount of hemoglobin Such a deficiency arises from diverse causes such as *chronic hemorrhage*, a *low dietary intake* repeated pregnancies and prolonged lactation rapid growth malabsorption or from any type of infection which may inhibit the utilization of iron salts A

*gratifying response usually follows iron therapy*

*It is now recognized that the nutritional* anemia of infancy and childhood chlorosis *or the hypochromic anemia of adolescent* girls the hypochromic anemia of pregnancy *the hypochromic anemia of chronic blood* loss and the idiopathic' hypochromic *anemia of adult women* are all varieties of the same condition which results from a *decreased supply of available iron in the* body These clinical syndromes have much *in common as they differ only because of the* age and sex of those affected

*Frequency*—These anemias are of the greatest importance because they occur at any age *in either sex and are one of the* most prevalent types observed in clinical *medicine An indication of their great* frequency is obtained from the studies of Davidson Fullerton and Campbell in 1935 in the poor of Scotland They found that such an anemia occurred in 41 per cent of the infants under two years of age 32 per cent of the children of pre-school age 16 per cent of adolescent girls and 45 per cent of adult women A study made at the University of Michigan Hospital several years ago showed that 39 per cent of all patients over 14 years of age admitted to the hospital or seen in the Out Patient Department who had an anemia had the iron-deficiency type

*Etiology*—Since iron is an essential part of the hemoglobin molecule (it is present in a percentage of 0 334) a deficiency in that metal will result in an iron-deficiency anemia A brief survey of iron metabolism is necessary to understand the causes of such a deficiency It is known that the average adult has in his body a total of about 4 2 grams of iron of which at least 55 per cent is in the hemoglobin of the circulating blood On an intake averaging from 10 to 15 milligrams a day one can provide his body with all the iron it needs and accumulate between 600 and 1000 milligrams of iron reserves held principally in the liver and reticulo endothelial system

Iron is taken into the body in the ferric form and acted upon by hydrochloric acid in the gastric juice to make it more soluble and prevent the formation of insoluble iron compounds It then passes into the intes*tine where it is reduced to the ferrous form* and absorbed as such Since iron is excreted *only in the bile and the urine and in amounts* averaging only 1 2 milligrams daily and the *iron intake is much larger it is apparent* that the amount of the metal in the body *must be regulated by an effective control of* its absorption It has been shown in *general that the body will absorb iron ef*ficiently when the reserves are low and reject *it entirely or in part when the reserves are* adequate When absorbed it combines with *apoferritin an iron free protein in the in*testinal wall to form ferritin It is then *distributed throughout the body as plasma* iron combined with globulin ($B_1$) This *protein is able to bind about 300 micro*grams of iron but is normally only about 35 *per cent saturated when iron-deficiency* anemia is present it may be only 10 per cent saturated (Finch)

The causes of iron depletion and iron deficiency anemia are as follows

1 *Loss of Blood*—Acute hemorrhage in an otherwise healthy person is rarely the cause of such an anemia for the iron reserves provide for the formation of from 1200 to 2000 cc of blood Chronic hemorrhage is the chief cause of such an anemia This occurs most commonly when there is a loss daily over long periods of small unnoticed quantities of blood For example a hemorrhage totaling only two teaspoonfuls of blood means the loss of 4 milligrams of iron Chronic hemorrhage is most commonly due to peptic ulcer and cancer of the stomach the large bowel the sigmoid and the rectum Other causes may be epistaxis bleeding from esophageal varices and more rarely bleeding from the small bowel as the result of enteritis benign tumor ulcer and vascular disease In women uterine bleeding is most commonly responsible for such an anemia

Since chronic bleeding is by far the most common cause of iron-deficiency anemia and probably the only single cause that results in such an anemia the rule should be when a microcytic hypochromic anemia is encountered to search at once for the source of blood loss In women despite the fact that they may insist that their menstrual periods are normal a common cause of such anemia is

the ankles *Pallor* as observed in the face is not always indicative of anemia, for the color of a person's skin is not entirely dependent on the hemoglobin level in the blood It is also concerned with the distribution and size of the skin capillaries, natural pigmentation sunburn, artificial coloring, and excessive fatigue Recently developing and persistent pallor however, is likely to be indicative of the presence of an anemia Usually the anemia can be detected more accurately by observing the mucous membranes or the palms of the hands

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Importance of an Accurate Diagnosis

An accurate diagnosis is absolutely essential in the management of various blood diseases If the anemia is detected by demonstration of a low hemoglobin, and a combination type of therapy instituted in the hope that the patient will improve, some good may be accomplished, but this method of therapy invites failure and does not provide an intelligent basis for establishing a prognosis A thorough history and physical examination must be done, along with a complete blood study, including an accurate hematocrit determination, to provide a basis for estimating the cell volume and hemoglobin content Additional studies as roentgen ray examinations, biopsy and sternal puncture may be necessary before the actual diagnosis is established

REFERENCES

Fowler W M Hematology 2d ed New York Paul B Hoeber Inc 1949
Handbook of Hematology Edited by Hal Downey New York Paul B Hoeber Inc Medical Book Department of Harper and Brothers 1938
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between 60 and 70 cubic microns and a Price-Jones curve with a pronounced shift of the peak to the left These findings indicate a hypochromic microcytic anemia which is almost always due to iron deficiency

The white blood cells are usually within normal limits but may be slightly reduced or occasionally be as low as 2000 per c mm Fresh *hemorrhage may produce a leukocytosis* with an increase in the percentage of neutrophils The blood platelets are usually normal but may be reduced in number They too may be increased in acute hemorrhage The recticulocytes are most frequently from 1 to 3 per cent but may be increased to 10 or 12 per cent following acute bleeding

*Bone Marrow* —The marrow is characteristically hyperplastic with a predominance of normoblasts often with a poverty of hemoglobin There is an approximate relationship between the number of these cells and the severity of the anemia Megaloblasts are absent but young normoblasts are not infrequently observed There is no important variation from normal in granulopoiesis Following specific therapy with iron the marrow returns to normal

Marrow preparations unstained or stained with Berlin blue normally show a considerable number of hemosiderin granules In the opinion of some observers (Rath and Finch 1948) this may be used as an index of the amount of iron stored in the tissues In iron-deficiency anemia diminution or absence of these granules may be observed

*Other Laboratory Findings* —The *blood bilirubin* is within normal limits as is the icterus index The *plasma proteins* and the albumin fraction may be reduced and account for edema in some patients This is probably chiefly due to low intake of protein *Achlorhydria* is usually present in the so-called idiopathic hypochromic anemia of women and occasionally in the hypochromic anemia of childhood in chlorosis the acidity is said to be normal or increased

*Iron* in the blood plasma is protein bound to $B_1$ globulin which holds 2 molecules of iron to one of protein In normal persons the total iron binding capacity is 300 gamma per 100 cc of serum but the circulating iron binding protein is only about 34 per cent saturated with iron In patients with iron-deficiency anemia it is usually below 10 per cent saturation (Rath and Finch, 1949)

## VARIOUS TYPES OF IRON-DEFICIENCY ANEMIAS

### Hypochromic Anemia of Infancy and Childhood (*Nutritional Alimentary* Chlorotic Anemia of Infancy)

This commonly occurring type of iron deficiency anemia is due to multiple etiologic factors as follows (1) A maternal iron deficiency which results in an infant being born with a normal hemoglobin of the blood but devoid of the usual iron reserves (2) Premature infants twins or those who for any other reason have a low birth weight may likewise have deficient iron reserves Rapid growth during the first year of life causes an increased demand for iron especially because the hemoglobin content of the body is doubled during this interval (3) A low iron intake due to prolonged artificial feeding exclusively with cow s milk which has a suboptimal iron content (4) Other factors may be infection anorexia achlorhydria or chronic diarrhea which interferes with the normal absorption of iron

This condition may in some instances be prevented by the administration of iron to the mother during pregnancy In the infant it responds promptly to this form of medication

### Chlorosis

*Definition* —An iron-deficiency anemia occurring in adolescent girls This is a disease limited to the adolescent female with the onset occurring usually between the ages of fourteen and seventeen years All evidence indicates that it is identical in every respect with the idiopathic hypochromic anemia of adult women except the age of onset and the presence of a normal amount of hydrochloric acid in the gastric juice Moreover as Richard Cabot said It takes the eye of faith to see the greenish yellow hue which such patients have been said to present in the past The characteristic blood changes are those of a hypochromic microcytic anemia Thayer reported 63 cases with a

profuse menstruation Three or four times the normal amount of menstrual blood may be lost each period without the patient's being aware of it

2 *Diminished Intake of Iron in the Diet* — This alone probably never causes an anemia although it may be an important contributing factor In infants and adolescents at the periods of rapid growth, a diet low in iron may result in such an anemia

3 *Increased demand for iron* due to rapid growth, pregnancy and lactation During periods of rapid growth as in infancy and at puberty and during pregnancy and lactation there is a notable increase in the body s demand for iron, hence it is at these times that iron-deficiency anemias are most likely to occur

4 *Malabsorption of Iron* —The efficiency of the absorption of iron is in part related to the amount of hydrochloric acid in the gastric juice Hydrochloric acid favors absorption achlorhydria has the effect of converting a diet high in iron to one low in iron Chronic diarrhea may also impair absorption

5 *Chronic Infection* —Chronic infection is associated with abnormal iron metabolism This is thought to result from the diversion of plasma iron to the tissues where it is not available for hemoglobin formation In the presence of an infection therefore excessive iron deposits appear to be made in the tissues but a relative iron deficiency seems to exist in the serum and red blood cells (Finch)

When bleeding, alone or in combination with other causes exhausts the iron reserves the body undoubtedly attempts to absorb more iron from the intestinal tract If this fails, the deficiency causes a hypochromic microcytic anemia, characteristic of iron deficiency

It should be reiterated that the most common cause of such an anemia is chronic hemorrhage usually from the gastrointestinal tract or the uterus Dietary deficiency increased demands due to growth pregnancy and lactation malabsorption and infection may play important roles in the etiology Whether any of these other than hemorrhage is the sole cause of such an anemia is doubtful

## Findings Common to All Iron Deficiency Anemias

*Symptoms* —The complaints of patients with an iron-deficiency anemia are similar to those of patients with any other type of anemia and are proportional to the degree of reduction of hemoglobin of the circulating blood Symptoms may be very mild or absent, especially in children but also in adults For example a healthy nurse, on active duty was admitted to the University of Michigan Hospital with a mild upper respiratory infection, and was unexpectedly found to have an iron-deficiency anemia with a hemoglobin of 50 per cent She insisted however that none of the symptoms of anemia were present and that she could work efficiently for eight hours daily without undue fatigue In most instances however definite chronic complaints are present although the patient does not appear acutely ill Ordinarily, the chief symptoms are weakness ease of fatigue pallor dyspnea on exertion palpitation a capricious appetite and vague digestive disturbances Physical examination usually discloses only a moderate loss of weight pallor often a hemic murmur and other features which are given under the heading of various types of iron deficiency anemia The fact that only a few positive findings are discovered on physical examination is important from the standpoint of diagnosis

*Blood Examination* —The most characteristic features are as follows (1) The pronounced decrease in the amount of hemoglobin contained in each red cell as indicated by a greater reduction in it than in the total red blood cell count For example a characteristic finding would be a red blood cell count of 3 500 000 per c mm and the hemoglobin of 35 per cent which gives a color index of 0 5 Other findings in accord with this are a mean corpuscular hemoglobin concentration usually varying from 25 to 30 per cent and a saturation index varying from 0 75 to 0 90 The mean corpuscular hemoglobin is within the limits of from 15 to 21 micromicrograms (2) There is a decrease in the size of the cells as indicated by mean diameter—usually between 6 2 and 6 7 microns mean corpuscular volume—usually

between 60 and 70 cubic microns and a Price-Jones curve with a pronounced shift of the peak to the left. These findings indicate a *hypochromic microcytic anemia* which is almost always due to iron deficiency.

The white blood cells are usually within normal limits but may be slightly reduced or occasionally be as low as 2000 per c mm. Fresh hemorrhage may produce a leukocytosis with an increase in the percentage of neutrophils. The blood platelets are usually normal but may be reduced in number. They too may be increased in acute hemorrhage. The reticulocytes are most frequently from 1 to 3 per cent but may be increased to 10 or 12 per cent following acute bleeding.

*Bone Marrow*.—The marrow is characteristically hyperplastic with a predominance of normoblasts often with a poverty of hemoglobin. There is an approximate relationship between the number of these cells and the severity of the anemia. Megaloblasts are absent but young normoblasts are not infrequently observed. There is no important variation from normal in granulopoiesis. Following specific therapy with iron the marrow returns to normal.

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*Other Laboratory Findings*.—The *blood bilirubin* is within normal limits as is the icterus index. The *plasma proteins* and the albumin fraction may be reduced and account for edema in some patients. This is probably chiefly due to low intake of protein. *Achlorhydria* is usually present in the so called idiopathic hypochromic anemia of women and occasionally in the hypochromic anemia of childhood; in chlorosis the acidity is said to be normal or increased.

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## VARIOUS TYPES OF IRON-DEFICIENCY ANEMIAS

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This commonly occurring type of iron deficiency anemia is due to multiple etiologic factors as follows: (1) A maternal iron deficiency which results in an infant being born with a normal hemoglobin of the blood but devoid of the usual iron reserves. (2) Premature infants, twins or those who for any other reason have a low birth weight may likewise have deficient iron reserves. Rapid growth during the first year of life causes an increased demand for iron especially because the hemoglobin content of the body is doubled during this interval. (3) A low iron intake due to prolonged artificial feeding exclusively with cow's milk which has a suboptimal iron content. (4) Other factors may be infection, anorexia, achlorhydria or chronic diarrhea which interferes with the normal absorption of iron.

This condition may in some instances be prevented by the administration of iron to the mother during pregnancy. In the infant it responds promptly to this form of medication.

### Chlorosis

*Definition*.—An iron-deficiency anemia occurring in adolescent girls. This is a disease limited to the adolescent female with the onset occurring usually between the ages of fourteen and seventeen years. All evidence indicates that it is identical in every respect with the idiopathic hypochromic anemia of adult women except the age of onset and the presence of a normal amount of hydrochloric acid in the gastric juice. Moreover as Richard Cabot said, "It takes the eye of faith to see the greenish yellow hue" which such patients have been said to present in the past. The characteristic blood changes are those of a hypochromic microcytic anemia. Thayer reported 63 cases with a

red blood cell count averaging about 4 000 000 per c mm and an average hemoglobin of 42 per cent Iron is specific in the condition, although it should be administered over a period of several months, and the patient observed for recurrences

It has been said that chlorosis has disappeared but apparently this is not the case if the above interpretation of the syndrome is accepted It is not unusual to see the mild form but the severe type is rare

### Hypochromic Anemia of Blood Loss

Detailed reference has been made to this syndrome under the heading of Etiology of the Iron-Deficiency Anemias It need only be reiterated here that this is one of the most common varieties of anemia encountered in the United States, and also undoubtedly in other parts of the world The blood findings in chronic blood loss are the typical ones observed in the iron-deficiency anemias and the therapeutic response to iron is prompt and satisfactory, unless the loss of blood is continued and excessive

### Hypochromic Anemia of Pregnancy

Observations have shown that a considerable number of otherwise normal pregnancies are accompanied by an iron deficiency It is unlikely that the gravid woman can retain a sufficient quantity of dietary iron to meet the demands of pregnancy which are occasioned by the added requirements of the fetal and maternal organism Moreover as the hydrochloric acid is diminished in many pregnant women this may result in an impaired absorption Preexisting reserves of iron in the body therefore must be called upon to satisfy the increased needs If these stores are depleted before pregnancy as they frequently are a further diminution will occur during the gravid state which will inevitably result in an iron-deficiency anemia unless suitable preventive or curative measures are instituted A second point to be considered is that the normally present increase in blood volume in pregnancy greatly augments any anemia which may exist as the result of other causes For example, the normal maximum blood dilution, as a result of hydremia, of 26 per cent usually occurs at about the sixth month If the hemoglobin percentage were 70 before the pregnancy, this dilution factor alone would reduce it to approximately 58 per cent

It is advisable that routine studies should be made as a part of prenatal care, and unless the values are unquestionably normal, iron medication should be given promptly and continued throughout gestation

### 'Idiopathic' Hypochromic Anemia

*Synonyms* —Simple achlorhydric anemia Simple achylic anemia Primary hypochromic anemia Chronic microcytic anemia Essential hypochromic anemia

*Definition* —A chronic microcytic, hypochromic anemia almost always occurring in women between the ages of twenty and fifty years who have an absence or reduced amount of free hydrochloric acid in the gastric juice The condition results from an iron deficiency in the body, attributable to diverse causes but chiefly to chronic hemorrhage and responds uniformly and favorably to iron therapy

*Etiology* —This syndrome is almost entirely limited to females although it has been reported occasionally in males According to Wintrobe and Beebe 60 per cent of the affected individuals are between thirty and fifty years of age while 82 per cent are twenty to fifty years These appears to be definite constitutional and hereditary trends in the disease and an ill-defined relationship to pernicious anemia Often there is a family history of anemia and families have been observed in which there have been cases of hypochromic anemia with achlorhydria some of which later changed to pernicious anemia and others which had the characteristics of pernicious anemia from the onset

There are four chief etiologic factors all of which may play a causative role in any given patient They are as follows (1) the most important is bleeding often unnoticed most frequently menorrhagia but also from other sources such as hemorrhoids and epistaxis (2) a deficiency of iron in the

diet (3) malabsorption of iron due to the achlorhydria or hypochlorhydria (4) frequent pregnancies at relatively short intervals

*Symptoms and Physical Examination* —The onset is gradual and the precise time of the initial appearance of symptoms is difficult to determine Usually the patient has been ailing for several years before consulting a physician In some instances the patient has apparently become adjusted to a low hemoglobin in the blood and consequently it may be surprising to find that the complaints are vague and relatively scant The symptoms are usually those associated with any anemia in which asthenia predominates Other complaints are mild chronic indigestion low resistance to respiratory infections emotional instability and vague neurotic pains Menorrhagia is common as on careful questioning it will be found that three-fourths or more of these women have an excessive loss of menstrual blood This is an important aspect of the history which is often overlooked unless particular attention is given to it A certain amount of glossitis and atrophy of the papillae of the tongue are present in about one third of the patients Rarely do these conditions attain the prominence observed in pernicious anemia Numbness and tingling of the extremities may be present but it differs from that of pernicious anemia as only 15 or 20 per cent of the patients have such a complaint and when present it is milder in degree and rarely as persistent When these *patients complain of dysphagia in addition* to the other symptoms the condition is then spoken of as the *Plummer Vinson syndrome*

Physical examination shows a variable degree of pallor either fair nutrition or moderate emaciation and frequently oral sepsis which probably bears no etiologic relationship to the disease In some cases there may be an acute glossitis with a tongue which appears intensely reddened while other patients may have no symptoms referable to the tongue but there may be atrophy of the papillae which gives the dorsum a smoothed-out appearance The finger nails may be dull lusterless and have longitudinal ridges A number of these patients have a peculiar concavity of the finger nails koilonychia ( spoon nails ) which usually affects the nails of several fingers but is most pronounced in the index finger The edge of the liver and the spleen may be palpable in a small number of patients These organs are never grossly enlarged In patients with severe anemia there may be pitting edema of the extremities The heart may be border line in size and a soft systolic apical ( hemic ) murmur is commonly present An important aspect of the physical examination is to exclude other conditions which might cause a similar anemia

*Blood* —The features are the characteristic ones of a microcytic hypochromic anemia In 90 per cent of the cases reported by Wintrobe and Beebe the red cells numbered between 3 000 000 and 5 150 000 per c mm and in 74 per cent the hemoglobin was 6 to 10 grams (38 to 64 per cent on the basis that 15 6 grams = 100 per cent)

*Gastric Analysis* —In about three fourths of the patients there is a failure to secrete hydrochloric acid in the gastric juice following the injection of histamine In the remainder there is almost always a hypochlorhydria

## TREATMENT AND PROGNOSIS OF IRON DEFICIENCY ANEMIAS

*Treatment* —Adequate doses of iron are specific in the iron-deficiency anemias The treatment of choice is ferrous sulphate 0 32 gram (5 grains) three times daily before meals A long trial has convinced me that *the enteric-coated tablets given before meals* will produce satisfactory results in almost all instances If gastrointestinal manifestations arise the preparation may be administered after meals and if necessary the dose reduced to one or two 0 32 gram (5 grain) tablets daily and the patient's tolerance determined Ordinarily a dose of 0 32 gram (5 grains) before meals is continued for two weeks *If there is not then a definite increase in the hemoglobin the dose should be doubled* If this dose does not cause a satisfactory response then (1) excessive hemorrhage may be causing the patient to lose blood faster than it can be formed (2) some infection renal disease (with increase in the nonprotein nitrogen of the blood)

hypothyroidism or vitamin C or protein deficiency may be complicating the case or (3) the patient may not be taking the preparation as advised

Other satisfactory iron preparations are ferrous gluconate (0 65 gram [10 grains] three times daily after meals) and ferrous carbonate (0 32 gram [5 grains] three pills taken three times daily with each meal) For children, the elixir of ferrous sulphate may be given in doses of 4 cc (0 12 gram 2 grains) three times daily after meals

Blood transfusions in these patients are useful for two reasons—because red blood cells and hemoglobin are actually given and because each 500 cc of blood contains 250 milligrams of iron The response to iron medication is so satisfactory, however that they are rarely indicated

Fatal poisoning from ferrous sulphate has been reported in infants after a gross overdose of tablets containing ferrous sulphate copper, and manganese (26 tablets) The subject is reviewed by Pram (1949) who suggests that destruction of the gastric mucosa by the excessive ferrous sulphate leads to lethal hepatic damage Parents should be warned to prevent children from taking a great many coated tablets of iron The possibility that harm may result from excessive amounts of iron given either intravenously as an iron preparation or as part of the hemoglobin molecule with blood transfusions must also be taken into consideration Such a complication as hemachromatosis is not likely to occur however till a dose of 25 grams has been given

In my experience it is usually not necessary to give other medication than iron Many patients with this type of anemia have an achlorhydria but the administration of dilute hydrochloric acid does not seem to enhance the utilization of iron importantly nor does it seem to be necessary to alleviate the gastric symptoms Although iron is not utilized efficiently except in the presence of small amounts of copper, there is enough copper in the patient s diet for this purpose and in addition, most iron preparations contain copper Vitamin supplements are not usually necessary unless there are special indications for their use, and special diets are not needed, except for patients with grossly abnormal dietary habits

With effective iron therapy there is usually a moderate rise in the reticulocytes of the peripheral blood within the first ten days, but it is less than that observed after effective therapy in patients with pernicious anemia Usually, at the beginning of the week there is a rise in hemoglobin This rise continues at the rate of about 1 per cent (0 15 to 0 2 gram) daily until the blood is normal

*Parenteral Iron* —Occasionally, when the patient is unable to tolerate iron orally, it is advantageous to give it parenterally Until recently iron could not be given by this route without risk of severe reaction There is now available a stable preparation saccharated oxide of iron, which appears to be satisfactory for intravenous use It has received extensive clinical trials especially in England and been found to be a safe and efficient preparation, easily administered without reaction *when given slowly* One preparation Ferrivenin' (Benger) used in England is prepared in 5 cc ampules containing 100 milligrams of elemental iron in a 2 per cent solution It is suggested that the contents of one ampule (100 milligrams of iron) will raise the hemoglobin 4 per cent hence the total amount required for a given patient may be approximated On the first day a dose of 1 5 cc may be given on the second day a dose of 3 cc on subsequent days doses of 5 cc until the blood is normal

*Prognosis* —This varies with the variety of hypochromic anemia In the nutritional anemia of children in chlorosis and idiopathic hypochromic anemia the effect of iron is prompt and all that is to be desired but there is an ever present tendency to a recurrence The latter condition frequently disappears after the menopause Iron medication should be continued for long periods of time and the patients observed until the periods of rapid growth or in the case of adolescent and adult women until there are no longer excessive demands for iron as those associated with menstruation pregnancy and lactation In the variety of anemia due to chronic hemorrhage the outlook is dependent upon the underlying cause of the bleeding The anemia is always amenable to iron

therapy if the loss of blood can be controlled and in the absence of an infection Even in cases of blood loss due to malignancy as with carcinoma of the stomach the anemia may often be corrected in part at least and the patient thereby greatly benefited temporarily


REFERENCES

FINCH C A Pathologic Physiology of Hemoglobin Formation Am Pract 1948 *3* 165

FOWLER W M and BARER A P Iron Metabolism and Its Relationship to Anemia and Therapy Ann Int Med 1940 *14* 378

GRANICK S Iron Metabolism and Hemochromatosis Bull New York Acad Med 1949 *25* 403

HEATH CLARKE W and PATEK ARTHUR J The Anemia of Iron Deficiency Medicine 1937 *16* 267

HYNES M Iron Metabolism J Clin Path 1948 *1* 57

SCHULTZE M O Metallic Elements and Blood Formation Physiol Rev 1940 *20* 37

SLACK H G B and WILKINSON J F Intravenous Treatment of Anemia with an Iron Sucrose Preparation Lancet 1949 *1* 11

RATH C C and FINCH C A Sternal Marrow Hemosiderin J Lab and Clin Med 1948 *33* 81

WINTROBE M M and BEEBE R T Idiopathic Hypochromic Anemia Medicine 1933 *12* 187


## PERNICIOUS ANEMIA

By CYRUS C STURGIS M D

*Synonyms* —Addisonian anemia Addison Biermer anemia Primary anemia

*Definition* —Pernicious anemia a chronic disease affecting both sexes equally but most commonly occurring in the white race in temperate climates at middle life or later is a macrocytic normochromic anemia with a megaloblastic bone marrow a persistent histamine resistant achlorhydria and frequently a recurrent glossitis and degenerative changes in the peripheral nerves and spinal cord The anemia is thought to be due to a failure of the gastric glands to secrete Castle s enzyme like intrinsic factor this failure results in lack of normal maturation of the red blood cells in the bone marrow There is a prompt response to specific therapy but untreated cases progress slowly usually with remissions to death

*Etiology* —Pernicious anemia is a relatively common disease in North America for of every 1000 patients admitted to a general hospital there are 3 or 4 with the disease The incidence has been given as 6 9 per 100 000 in the United States 9 1 in Canada, and 9 18 in Sweden (Askanazy 1937) The apparent increase in the prevalence of the condition is due undoubtedly to more accurate methods of diagnosis and to the fact that as the result of increased longevity a greater number of persons now live to the age when the disease commonly occurs

This variety of anemia unquestionably has a greater incidence in certain races than in others It is observed frequently in the United States Canada England Scotland Ireland and the countries of Northern Europe whereas it is rarely seen in natives of the tropics China or South America It probably never occurs in pure blooded Negroes but has been observed in mulattoes It is distinctly a disease of the white race in temperate climates

Symptoms develop most frequently between forty and sixty five years of age If a group of patients with pernicious anemia are considered according to their age and the number of individuals living at the various ages however the highest incidence is between sixty five and seventy years True pernicious anemia probably never develops in young children but the onset may occasionally be during the second decade of life It is not rare in individuals between twenty and thirty years of age Cases have been reported in infants and young children but they probably have had the megaloblastic anemia of infancy a disease which differs from pernicious anemia in several important aspects

The two sexes are affected with equal frequency

The hereditary occurrence of pernicious anemia is now an established fact A familial incidence of between 10 and 20 per cent is the one usually given but it is probably higher It has been reported in identical twins and as many as five cases have been observed in siblings Not only are outspoken cases of pernicious anemia observed in the same family but a number of the other immediate relatives may have achylia gastrica recurrent glossitis or minor changes

hypothyroidism or vitamin C or protein deficiency may be complicating the case or (3) the patient may not be taking the preparation as advised

Other satisfactory iron preparations are ferrous gluconate (0.65 gram [10 grains] three times daily after meals) and ferrous carbonate (0.32 gram [5 grains] three pills taken three times daily with each meal) For children, the elixir of ferrous sulphate may be given in doses of 4 cc (0.12 gram 2 grains) three times daily after meals

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glands in the mucosa of the cardiac end of the stomach the area of principal atrophy in patients with pernicious anemia secrete the intrinsic factor as well as hydrochloric acid and pepsin In various species however the site may be different The cause of the functional failure of the gastric glands is obscure

The cause of the changes in the nervous system is not known, but the knowledge that is available concerning their etiology plus the recent information which has been acquired in regard to the vitamins suggests that a deficiency of a vitamin or a vitamin like material perhaps related to the B complex, a more pronounced deprivation might produce changes in the lateral columns It is certainly true that the neurologic manifestations invariably advance in a set order which suggests first peripheral nerve involvement, next changes in the posterior column, and finally lateral column lesions

*Pathology* —No single pathologic change is recognized as characteristic of pernicious anemia The most constant anatomic findings are the anemia widespread fatty degeneration of many parenchymatous viscera and the muscles hyperplastic changes in the bone marrow with the megaloblasts as the predominating cells degenerative



Fig 181 —Cross section of the spinal cord (Sturgis Diseases of the Blood courtesy of Charles C Thomas )

may play the leading role in the causation of these lesions The persistent achlorhydria in patients with pernicious anemia may be an important factor in the production of this, as absorption may be impaired and thereby cause a vitamin insufficiency despite an adequate dietary intake It is plausible that a total or partial lack of some substance acting with varying degrees of intensity over a long period might produce different neurologic changes thus the earliest evidence of a shortage could be changes in the peripheral nerves associated with paresthesia of the extremities a further intensification of the deficiency might then cause lesions of the posterior column and finally changes in the peripheral nerves, and similar lesions involving the posterior and lateral columns of the spinal cord The process is thought to attack first the myelin sheaths at which time it is probably a reversible condition the later destruction of the axis cylinders is probably a permanent change Unless anti pernicious anemia therapy has been given there is an absence of glial activity

Gastroscopic and observations at necropsy indicate that atrophic gastritis is present in patients with pernicious anemia and combined degeneration of the cord The involvement is chiefly in the region of the fundus In this area the specific glandular

in the blood, suggesting an early or incomplete type of pernicious anemia. It is generally accepted that achlorhydria, and probably a diminution of the intrinsic factor, are often *hereditary precursors of pernicious anemia*. There is no evidence to indicate that the disorder is sex linked or sufficient data to permit a conclusion as to whether the trait for the disease is dominant or recessive.

Any statement now made concerning the etiology of pernicious anemia must be considered purely tentative. New information is being accumulated so rapidly that overnight our views may be revised radically. With the available information, however, *the theory advanced by Castle in 1929* appears plausible provided certain modifications are accepted. This observer has demonstrated that an unidentified substance in the diet (the extrinsic factor) when taken into the stomach reacts with an enzyme-like material in the gastric secretions (the intrinsic factor) to produce a product essential to the development of the red blood cells in the bone marrow. In pernicious anemia, the intrinsic factor is diminished, *hence maturation of the red blood cells in* the bone marrow does not proceed normally.

Observations in recent years have amplified this theory, but nothing has been discovered to date which is incompatible with the fundamental principles elaborated by Castle. It is now recognized that the normal diet contains at least two materials necessary to the development of the red blood cells—pteroylglutamic acid (folic acid) and vitamin $B_{12}$. There is strongly suggestive evidence, however, to indicate that neither is in food in readily utilizable form: folic acid is in the conjugated or inactive form, and vitamin $B_{12}$ must *also be activated or altered in some manner*.

It has been suggested by Hall, Bethell and their associates *that the change produced* in vitamin $B_{12}$ is accomplished by the intrinsic factor, which (1) makes it absorbable by changing its physical or chemical characteristics, (2) prevents its destruction by gastrointestinal secretions or (3) averts the deleterious effects which may be produced by intestinal bacteria. The role played by "apoerythein," the heat labile substance in normal gastric juice, is uncertain. Ternberg and Eakin, who discovered it in 1949, *demonstrated that this* material combines with vitamin $B_{12}$ to make the latter unavailable for the growth of certain bacteria.

Once $B_{12}$ and conjugated folic acid are absorbed by the body, the events leading to their actions in the development of the red blood cells in the bone marrow are not known. The vitamin may convert the inactive conjugated form of folic acid into its free and active type, but there are certain *objections to this theory. If this did occur, it* could be assumed that the liberated folic acid supplied the necessary stimulus to the development of the red blood cells in the bone marrow and that, under the influence of the required amount of this material, they matured at a physiologic rate which maintained the red blood cell count of the circulating blood at a normal level.

If such a theory were accepted, it must be acknowledged that the primary cause *of pernicious anemia is a reduced rate* of production of red blood cells in the bone marrow and that the increased destruction of erythrocytes in the disease was of secondary importance. This concept assumes that pernicious anemia is due to the body's inability to absorb or utilize vitamin $B_{12}$ normally, which results from a deficiency of intrinsic factor in the gastric juice. The result would be failure to convert the diet's conjugated folic acid into free and active folic acid. Assuming the latter is essential to the normal rate of development of the red blood cells, reduced production of red blood cells in the bone marrow would follow, together with the development of an anemia due to diminished erythrocyte formation.

*No available information* indicates the ultimate cause of the intrinsic factor deficiency. It seems logical to attribute it, however, to some inherited defect of the stomach. Clinical observations have shown that a chronic gastritis commonly occurs during the disease but disappears during remissions. Furthermore, careful studies in *man have demonstrated* an atrophy of the upper two thirds of the gastric mucosa which ends sharply at the junction with the pyloric region. It appears probable *that the*

glands in the mucosa of the cardiac end of the stomach the area of principal atrophy in patients with pernicious anemia, secrete the intrinsic factor as well as hydrochloric acid and pepsin In various species however the site may be different The cause of the functional failure of the gastric glands is obscure

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*Fig 181* —Cross section of the spinal cord (Sturgis Diseases of the Blood courtesy of Charles C Thomas )

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It was recognized many years ago by Hunter that the liver kidneys and spleen may contain deposits of hemosiderin, an iron-containing pigment which is derived from hemoglobin

Peabody, by means of biopsies, observed that during relapse the essential histologic lesions in the bone marrow is a proliferation of megaloblasts which results in a hyperplastic but functionally inefficient marrow as these cells fail to differentiate toward mature erythrocytes This state has been designated as a maturation arrest During a remission there is a great relative increase of normoblasts and mature red blood cells in the marrow whereas the megaloblasts are rare Sternal puncture in a patient with pernicious anemia in relapse shows a pre




Fig 183 —Nucleated red cells E Erythroblasts (1 2 and 3) The cells are large the cytoplasm is basophilic and the chromatin of the nucleus is disposed in strands These cells are younger than normoblasts N Normoblasts The cells are smaller and the cytoplasm is less basophilic than the erythroblast The chromatin of the nucleus is dense or pyknotic In 4 and 5 the nucleus is being extruded In 1 2 and 6 the nucleus is breaking up as indicated by the fleur de-lis shape (Haden s Principles of Hematology )

dominance of megaloblasts and their progenitors Following treatment there is a prompt change, even after a single day by which time most of the cells are in a middle or advanced stage of maturation There is also a rapid transition to normal in the neutrophils following therapy

*Symptoms* — These may be divided into four groups depending on whether they are referable to the anemia the gastro intestinal tract the nervous system or the cardio vascular system In a very large percentage of patients there are usually manifestations of varying degree representing each group According to Minot the earliest complaints are referable to the anemia in 33 per cent of the patients to the digestive tract in 31 per cent to the nervous system in 26 per cent, and the heart in 10 per cent The important symptoms which are due to the anemia are weakness ease of fatigue pallor and dizziness Those associated with the gastro intestinal system are anorexia recurrent attacks of glossitis, nausea, vomiting mild epigastric discomfort and either constipation or diarrhea, or an alternation of the two It should be emphasized that about 12 per cent of patients with pernicious anemia have associated gall bladder disease which should always be suspected in the presence of persistent abdominal complaints especially if they continue after adequate anti pernicious anemia therapy has been given The most common evidence of in

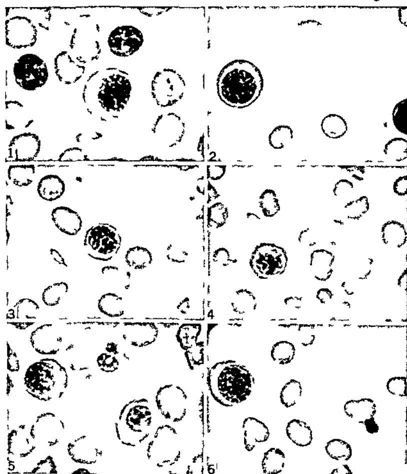



Fig 184 —Nucleated red cells Megaloblasts The cells are large with basophilic cytoplasm *The chromatin is loosely arranged often giving a cart-wheel appearance* The cells in 1 2 4 and 6 are from a patient with myeloblastic leukemia those in 3 and 4 are from a patient with erythroblastic anemia (Haden s Principles of Hematology )

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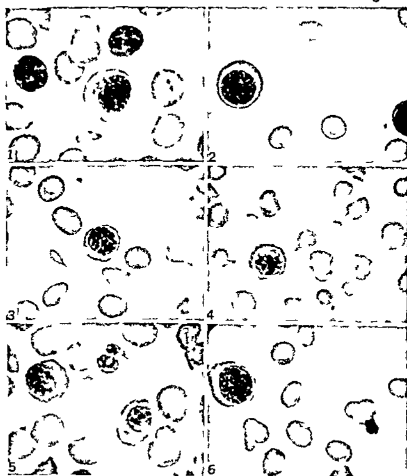



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regardless of the amounts of specific therapy given The hemoglobin during a relapse shows a drop which is less than the red blood-cell count, and as a result the color index is 1 or greater A high color index is constantly observed in uncomplicated pernicious anemia

The most characteristic finding in a stained blood film is the presence of large, round or oval red blood cells which are well filled with hemoglobin These macrocytes as they are called may make up 25 to 30 per cent of all the red blood cells and parallel in number roughly the severity of the anemia In addition there are present a variable number of small red blood cells microcytes which may measure only 3 or 4 microns in diameter Poikilocytosis or irregularity in shape of the red blood cells is almost always observed when the anemia is severe There is an increase in the mean corpuscular volume to between 100 and 130 cubic microns, the mean corpuscular hemoglobin concentration to between 32 and 35 per cent and the mean corpuscular hemoglobin from 30 to 52 micromicrograms Measurement of the diameters of the erythrocytes by the Price-Jones procedure shows a characteristic curve when an anemia is present The greatest percentage of red blood cells measure between 9 and 9 5 microns but there is an extreme variation in the size which may range from 3 5 to 14 microns While the measurement curve which is seen in pernicious anemia may also be present in other macrocytic anemias it is wholly different from that observed in the blood of patients with normocytic or iron-deficiency anemias

Various forms of immature red blood cells may be present such as normoblasts megaloblasts cells showing diffuse basophilia or stippling and less frequently Howell Jolly bodies and Cabot s ring forms With a special vital stain such as cresyl blue reticulocytes may be demonstrated but in relapse they are rarely present in numbers greater than 1 per cent of the red cells It should be emphasized that immature red blood cells in the peripheral blood are not essential to the diagnosis of pernicious anemia They appear only when the patient is improving and the red blood-cell count is rising

There is practically always a reduction in the number of platelets A reduced white-blood cell count is characteristic of pernicious anemia during a relapse It is exceedingly rare to observe a leukocytosis even with an active infection when the red blood-cell count is low With antipernicious anemia treatment, however the leukocyte count may be excessively high in the presence of an infection

*Other Laboratory Tests —Gastric Analysis* —One of the most important laboratory procedures from the standpoint of diagnosis is an examination of the gastric contents for free hydrochloric acid In our series of almost two thousand patients at the Simpson Memorial Institute in whom a fractional gastric analysis was done there was a complete absence of hydrochloric acid in every single case and a uniformly low total acidity Three to five specimens were removed in each instance and in practically all of the patients the analysis followed the injection of 0 5 to 1 mg of histamine intramuscularly Not only does the achlorhydria exist at the time the clinical manifestations of pernicious anemia are apparent but it is now well established that it may be present many years prior to their appearance and probably exists from birth It is known also that the absence of free hydrochloric acid persists when the blood returns to normal and also when the patient is symptomless either as a result of a spontaneous or therapeutically induced remission The facts regarding the achlorhydria of pernicious anemia are so well established that the presence of free hydrochloric acid in the gastric contents of a patient who is suspected of having pernicious anemia practically eliminates this diagnosis regardless of other convincing evidence of the disease In addition to the lack of free hydrochloric acid pepsinogen (the precursor of pepsin) is rarely if ever present in the gastric contents

*Hyperbilirubinemia* —It is well established that the bilirubin content of the blood serum is always increased when the red blood-cell count is low and that it falls to normal as the red cell count rises While it may not be accepted that the amount of bilirubin in the

volvement of the nervous system is numbness of the hands and feet, weakness and spasticity of the muscles of the lower extremities, ataxia which is due to the loss of the sense of motion and position of the lower extremities and loss of control of the sphincter of the bladder Cardiovascular manifestations due mainly to the anemia are dyspnea on exertion palpitation sometimes edema of the ankles, and occasionally, the cardiac pain characteristic of angina pectoris

*The history of the average case is one of* gradually developing weakness in a person of middle age which becomes progressively worse until it is often completely incapacitating Coincident with the development of this symptom, pallor, sometimes with a yellowish tint, dyspnea and palpitation on exertion and occasionally edema of the ankles are observed About 90 per cent of the patients complain of numbness and tingling of the hands and feet It is important to note that this almost always involves all four extremities, and it is persistent, although it may vary in intensity Recurring attacks of sore tongue occur in more than one-half of the patients and in rare instances it is the initial and outstanding symptom This complaint may be only a mild burning discomfort or an extensive involvement which may interfere seriously with the ingestion of food As the anemia becomes pronounced, nausea vomiting fever and delirium may appear

*Physical Examination* —Usually reveals a fairly well nourished individual, although there is commonly a loss of 10 to 20 pounds in body weight during the illness A pronounced pallor which may have an associated yellowish tint may be present thereby giving rise to the so called lemon yellow or grape fruit appearance to the skin and conjunctiva this is observed much less commonly now than in the past The hair is usually partly or completely gray and the eyes are most frequently colored the lighter shades of green or blue Not infrequently the tongue over the dorsum, has a smooth appearance due to atrophy of the papillae In some instances it may be a fiery red as a result of the associated glossitis Rarely is the tongue coated during the period of severe anemia in fact, a heavily coated tongue casts some doubt on the diagnosis of pernicious anemia The lungs are usually normal and the heart shows no conspicuous changes except that frequently a soft systolic (*hemic*) *murmur* is present, and there may be borderline enlargement of the left ventricle The spleen and liver are rarely palpable The presence *of splenomegaly at once suggests some other* disease than pernicious anemia Not infrequently the abdomen is distended which may be a troublesome symptom especially in patients with spinal cord involvement A slight to moderate edema of the ankles may be present when the red blood cell count is below 2 000 000 per c mm When the anemia becomes severe a hemorrhagic tendency associated with a diminution in platelets may develop as evidenced by petechiæ and ecchymoses retinal hemorrhages epistaxis and bleeding from other sources Objective evidence of degenerative changes in the posterior and lateral columns of the spinal cord is commonly encountered Those due to posterior column involvement are loss of vibratory sense and the sense of motion and position of the lower extremities ataxia and a positive Romberg sign Changes in the lateral columns are responsible for evidences of spastic paraplegia exaggerated knee jerks and a bilateral positive Babinski sign Not infrequently cerebral manifestations such as mild depression irritability impaired memory occasionally delusions and hallucinations and even maniacal outbursts may be present

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regardless of the amounts of specific therapy given. The hemoglobin during a relapse shows a drop which is less than the red-blood-cell count, and as a result the color index is 1 or greater. A high color index is *constantly observed in uncomplicated pernicious anemia*.

The most characteristic finding in a stained blood film is the presence of large, round or oval red blood cells which are well filled with *hemoglobin*. These *macrocytes, as they are called*, may make up 25 to 30 per cent of all the red blood cells and parallel in number roughly the severity of the anemia. In addition, there are present a variable number of small red blood cells, *microcytes*, which may measure only 3 or 4 microns in diameter. Poikilocytosis, or irregularity in shape of the red blood cells, is almost always observed when the anemia is severe. There is an increase in the mean corpuscular volume to between 100 and 130 cubic microns, the mean corpuscular hemoglobin concentration to between 32 and 35 per cent, and the mean corpuscular hemoglobin from 30 to 52 *micromicrograms*. Measurement of the diameters of the erythrocytes by the Price-Jones procedure shows a characteristic curve when an anemia is present. The greatest percentage of red blood cells measure between 9 and 9.5 microns, but there is an extreme variation in the size which may range from 3.5 to 14 microns. While the measurement curve which is seen in pernicious anemia may also be present in *other macrocytic anemias, it is wholly different* from that observed in the blood of patients with normocytic or iron-deficiency anemias.

Various forms of immature red blood cells may be present, such as normoblasts, megaloblasts, cells showing diffuse basophilia or stippling, and less frequently *Howell-Jolly bodies and Cabot's ring forms*. With a special vital stain, such as cresyl blue, reticulocytes may be demonstrated, but in relapse they are *rarely present in* numbers greater than 1 per cent of the red cells. It should be emphasized that immature red blood cells in the peripheral blood are not essential to the diagnosis of pernicious anemia. They appear only when the *patient is improving* and the red blood-cell count is rising.

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responds to treatment with crude liver extracts autolyzed yeast extracts and folic acid Relapses do not occur if the diet is corrected

*Refractory megaloblastic anemia* as described by Davidson (1948) is a macrocytic anemia with megaloblastic hyperplasia of the bone marrow It occurs in both sexes and in persons between 12 and 70 plus The symptoms and signs are usually only those of a severe anemia Acute glossitis is rare but the chronic form of the complaint is common There are no objective signs of involvement of the central nervous system In slightly over half the *patients there is a histamine-resistant achlorhydria* and in these the differential diagnosis from pernicious anemia is impossible until it is demonstrated that there is failure to respond to parenteral injections of liver extract According to Davidson (1948) these cases would conform to the condition designated as *Achrestic anemia* by Israels and Wilkinson (1936) Proteolyzed liver or folic acid apparently has been employed successfully for this condition at least it is worth a thorough trial It is suggested that possibly this anemia is associated with a dietary deficiency (of conjugated folic acid) malabsorption of some essential dietary constituent or some disturbance in liver function (Davidson)

A macrocytic anemia may occur in patients who have had *total gastrectomy intestinal anastomoses or strictures* This is due either to removal of the intrinsic factor to malabsorption or to stagnation of the intestinal contents probably with some alteration in the intestinal flora Glossitis and neurological changes may be present Response is obtained to liver extract or vitamin $B_1$ given parenterally or to folic acid given parenterally or orally In patients with intestinal disturbances the intrinsic factor is present in the stomach

A small percent possibly a third of the cases with *cirrhosis of the liver* have a macrocytic anemia The rest have a normocytic or microcytic anemia probably dependent on the amount of hemorrhage There is a leukopenia or a normal white blood-cell count The platelet count is low normal or distinctly diminished There is usually a macronormoblastic erythropoiesis in the bone marrow A megaloblastic marrow may occur but it is rare The pathogenesis of the anemia in cirrhosis of the liver independent of bleeding is obscure Failure of adequate storage of the erythrocyte-maturing factor has been suggested as a cause of the macrocytic anemia but this view is not entirely acceptable for this factor has been demonstrated in the livers of patients succumbing to the disease The possibility that the anemia may be on a nutritional basis must be considered since patients with cirrhosis almost always eat a deficient diet, usually one low in protein Liver extract given parenterally and folic acid *given orally or parenterally* may be used therapeutically but they do not always produce satisfactory results The differential diagnosis of pernicious anemia from cirrhosis should not be difficult in cirrhosis neurological involvement is absent ascites may be present cutaneous angiomas are indicative of extensive hepatic involvement and liver function tests are positive

A macrocytic anemia with megaloblastic hyperplasia of the bone marrow may be due to infestation with the *broad tapeworm diphyllobothrium latum* (which occurs most frequently in Finland but patients may occasionally acquire the infestation in North America) The anemia and the bone marrow changes are identical with those observed in true Addisonian pernicious anemia A histamine resistant achlorhydria is usually present but free acid may be detected in persons under twenty years of age Neurological changes are not observed The associated anemia occurs in far below one per cent of the cases of the infestation Apparently the cause of the anemia is an interference in some obscure way with the interaction between the extrinsic and intrinsic factors Prompt control of the anemia can be accomplished by the injection of liver extract or folic acid even when the parasite remains in the intestinal tract The simplest method of treatment however is removal of the worm It should be kept in mind that in a country such as Finland where both the infestation and pernicious anemia are common patients may be encountered with true pernicious anemia in whom the parasite is also present

serum is an index of the degree of blood destruction nevertheless it is a fairly good index of the course of the disease and as an aid to diagnosis There are two clinical methods for estimating the bilirubin in the blood serum These are the van den Bergh reaction and the icterus index The upper limit of normal for the former test is 0 7 mg of bilirubin per 100 cc of serum, whereas the normal limits of the icterus index are expressed in the arbitrary figures 4 to 6 In pernicious anemia during relapse the icterus index averages between 20 and 25 and the indirect van den Bergh reaction gives *a reading averaging from about* 1 0 *to* 1 5 mg per 100 cc of blood although occasionally higher figures are noted

*Diagnosis* —Ordinarily the diagnosis of pernicious anemia is not difficult If an adult complains of the usual symptoms of an anemia such as weakness pallor dyspnea and palpitation, and there is a yellowish tint *to the skin and conjunctiva the most* likely diagnosis is pernicious anemia If additional complaints include persistent numbness of the hands and feet and recurrent attacks of glossitis and a histamine resistant achlorhydria is present the diagnosis is almost certain even before the blood is examined Other findings which are helpful *are the characteristic blood picture* hyperbilirubinemia a history of remissions and findings suggesting subacute combined degeneration of the spinal cord It is of assistance to keep in mind that there are seven cardinal points of fundamental diagnostic importance in relation to pernicious anemia and if all or even a majority are present the diagnosis is at once suggested or established These are (1) achlorhydria (2) macrocytosis (3) a high color index and normal mean corpuscular *hemoglobin* concentration (4) paresthesia of all four extremities, (5) recurrent glossitis (6) leukopenia and (7) a favorable response to antipernicious anemia therapy

## Macrocytic Anemia Other than Pernicious Anemia

*Differential Diagnosis* —A number of conditions, in addition to pernicious anemia are characterized by a macrocytic anemia with megaloblastic hyperplasia of the bone marrow It is impossible to differentiate them from pernicious anemia by examination of the blood and bone marrow alone These are the macrocytic anemias associated with (1) sprue, (2) pregnancy and the *puerperium* (3) *deficient nutritional states* (4) refractory megaloblastic anemia (Achrestic anemia) (5) total gastrectomy intestinal anastomosis, and stenosis (6) cirrhosis of the liver, (7) megaloblastic anemia of infancy, and (8) fish tapeworm infestation

*Sprue* and the closely allied conditions, idiopathic steatorrhea and coeliac disease in infancy are often associated with a macrocytic anemia and a megaloblastic bone marrow In these conditions especially in sprue the stools are voluminous foamy greasy, liquid gray in color and foul in odor About half the patients have an achlorhydria There are no neurological changes There may be a recurrent glossitis Liver extract and $B_{12}$ given parenterally are highly effective in the treatment of this disease as is folic acid administered orally or parenterally with a diet high in protein There is a tendency to relapse when the treatment is discontinued

*Macrocytic anemia of pregnancy* occurs usually in women under forty years of age Free *hydrochloric acid is present in the* gastric secretions in about half the cases Glossitis and neurological manifestations are absent Recovery follows treatment with folic acid or disappears after the termination of pregnancy The most efficient form of therapy is with folic acid although some improvement may follow the use of liver extract The disease apparently is refractory to treatment with $B_{12}$ (Bethell)

*Nutritional macrocytic anemia* may occur *in any patient on a persistently abnormal* diet especially one deficient in protein This condition has been observed most commonly in the tropics It may occur at any age between the late teens and relatively old age (Wills) The patients are usually emaciated edema may be present the neurological manifestations are absent The exact cause of the condition is not clear but it probably is due to absence in the diet of some factor necessary for the normal rate of formation of red blood cells in the bone marrow It

the greatest therapeutic problem since the introduction of liver therapy and it is easily the most important single factor in estimating the prognosis Approximately 85 per cent of our patients showed improvement in their neurologic manifestations when *treated efficiently* with a refined, concentrated liver extract intramuscularly and in only 2 per cent was there an advance in the symptoms On the other hand only 28 6 per cent of the patients in whom the treatment had been *inadequate* exhibited improvement, and 28 5 per cent showed an unfavorable progression

It is of great importance from the standpoint of prognosis to consider the extent and duration of the neurologic lesions Often these have the same meaning that is the longer the duration the greater the extent of the changes But this is not necessarily true as for example an extensive subacute combined degeneration may develop within a few weeks or sometimes paresthesias of the extremities may be the only evidence of involvement of the nervous system for several years In general after they have been present for more than one year it is agreed that there is a decreased prospect of improvement although it is believed by some that they may diminish in severity even after they have been present for as long as four years

Although it is agreed that a high degree of functional recovery may occur even when the pathologic changes are extensive it must be kept in mind that there is some correlation between the magnitude of the neurologic lesions and the prognosis Thus patients with paresthesias and posterior column spinal cord changes have a less favorable outlook than those without neurologic symptoms or with paresthesias only Those with combined degeneration of the spinal cord especially when they are associated with functional impairment of the urinary bladder usually survive the shortest period of time The characteristic course of events in patients with bladder complaints leading to a fatal termination is as follows retention of urine with distention of the bladder which invariably leads to a cystitis and eventually an ascending infection of the urinary tract Abscesses of the kidney with septicemia and death due to a complicating bronchopneumonia may follow These changes pertain to the course of the disease in the average patient It should be remembered however, that there have been some remarkable instances of long period of survival of patients with advanced spinal cord changes

*Treatment of Pernicious Anemia and Other Macrocytic Anemias* —The most effective treatment of pernicious anemia is by intramuscular injection of a refined U S P liver extract containing 15 units per cc Treatment with vitamin $B_{12}$ however may prove equally effective Both are complete treatments, that is they favorably affect the anemia the glossitis and the neurological manifestations

A patient with the disorder in relapse should be given intramuscularly daily for one week 1 cc of refined liver extract containing 15 units * The same dosage is continued three times weekly for the next two weeks and thereafter twice weekly When the hemoglobin reaches 13 grams per 100 cc of blood and the red blood-cell count 4 5 million per cubic millimeter a maintenance dosage is given this should be continued throughout the patient s life With refined liver extract the average adequate maintenance dose is 1 cc containing 15 U S P units, given intramuscularly every two weeks or 2 cc containing 30 units given intramuscularly every 4 weeks The dosage of vitamin $B_{12}$ may be estimated on the basis that one microgram of the vitamin equals approximately one unit of liver extract

The first evidence of improvement after antipernicious anemia medication is seen in from three to six days There are a striking increase in appetite a rapid disappearance of gastrointestinal complaints a fall in the body temperature and pulse rate to normal and a gain in strength which often permits the patient to resume normal activities in from four to eight weeks The earliest change in the blood is an increase in the immature red blood cells or reticulo-

* A unit of liver extract is that amount which produces when administered daily a satisfactory clinical and hematopoietic response in Addisonian pernicious anemia

The *megaloblastic anemia of infancy,* characterized by a macrocytic anemia with megaloblastic hyperplasia of the bone marrow, usually occurs in infants under 18 months of age Recovery generally follows therapy with one course of liver extract or folic acid The nervous system is not involved, and there is a marked hypoacidity of the gastric juice, or achlorhydria The outstanding feature of this disease and that which distinguishes it from true Addisonian pernicious anemia is the cure by one course of treatment (there is no relapse despite discontinuance of therapy) The most likely cause is a deficiency of folic acid (Luby and Wheeler, 1949) due to dietary deficiency and the influence of infection, which may decrease the folic acid reserves of the body, lower the intake (by creating anorexia), prevent absorption (by causing diarrhea), and possibly reduce bacterial synthesis of folic acid in the intestinal tract It is suggested by Zuelzer that 20 milligrams of folic acid be given by daily parenteral injections for a week, although doses of as little as 5 milligrams a day given orally have proved adequate Liver extract in doses of 15 USP units or vitamin $B_{12}$ 15 units given parenterally and repeated as often as necessary, apparently yield satisfactory results

The following conditions should be listed as possible causes of a macrocytic anemia and ones which should be considered in the differential diagnosis of pernicious anemia They do not, however cause megaloblastic hyperplasia of the bone marrow but a condition that is either normoblastic or macronormoblastic These conditions in which the red blood cell volume (M C V) may be between 96 and 120 cubic microns but rarely exceeds 110 cubic microns, are as follows (1) myelophthisic anemia the most important causes of which are subleukemic leukemia and Hodgkin's disease (2) myxedema (3) hemolytic anemia (4) aplastic anemia and (5) acute hemorrhage Nephritis is sometimes given as a cause of a macrocytic anemia, but this is seldom true The anemia associated with nephritis is normocytic and normochromic

*Prognosis* —Prior to the introduction of modern methods of treatment, pernicious anemia was rightly considered to be an invariably fatal disease from which the average patient succumbed within two to three years In most instances, however there were spontaneous remissions which persisted for three to six months but the general trend of the disease was invariably downward Occasionally a patient survived for five or six years, and rarely as long as fifteen or twenty years

With the introduction of specific anti pernicious anemia therapy, the outlook has been completely changed and, theoretically at least, a patient with proper treatment should live for his normal span of life or die of some unrelated condition Certainly the prognosis is much more promising as indicated by the statistics of the Metropolitan Life Insurance Company, which show that the disease is now responsible for about 7000 fewer deaths a year in the United States than it was 20 years ago and that there has been a decrease of 80 per cent in the death rate as a result of the modern treatment at the ages of 45 to 75 years, where the mortality of the disease is concentrated With additional improvement in specific medications and their methods of administration, constant betterment in the outlook of patients with this disease is to be anticipated

The most important factors in the prognosis are the effectiveness with which the anti pernicious anemia medication is given, the state of the nervous system the occurrence of infections and the fact that an increased dosage is required in older patients or those with arteriosclerotic changes The most common cause for failure is the unnecessary and regrettable tendency of the patient to become lax in taking treatment Usually the ensuing relapse is not complete but it may be of such an extent that the neurologic lesions progress to an irreversible state It is of first importance in combating this to prescribe an amount of medication which is somewhat in excess of the minimal dosage necessary to keep the blood within normal limits and to insist that each patient report at least every three months for a complete blood examination

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the greatest therapeutic problem since the introduction of liver therapy and it is easily the most important single factor in estimating the prognosis. Approximately 85 per cent of our patients showed improvement in their neurologic manifestations when *treated efficiently* with a refined concentrated liver extract intramuscularly, and in only 2 per cent was there an advance in the symptoms. On the other hand only 28.6 per cent of the patients in whom the treatment had been *inadequate* exhibited improvement, and 28.5 per cent showed an unfavorable progression.

It is of great importance from the standpoint of prognosis to consider the extent and duration of the neurologic lesions. Often these have the same meaning, that is, the longer the duration, the greater the extent of the changes. But this is not necessarily true as, for example, an extensive subacute combined degeneration may develop within a few weeks, or sometimes paresthesias of the extremities may be the only evidence of involvement of the nervous system for several years. In general, after they have been present for more than one year it is agreed that there is a decreased prospect of improvement, although it is believed by some that they may diminish in severity even after they have been present for as long as four years.

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*Prognosis.*—Prior to the introduction of modern methods of treatment pernicious anemia was rightly considered to be an invariably fatal disease from which the average patient succumbed within two to three years. In most instances, however, there were spontaneous remissions which persisted for three to six months but the general trend of the disease was invariably downward. Occasionally a patient survived for five or six years, and rarely as long as fifteen or twenty years.

With the introduction of specific antipernicious anemia therapy the outlook has been completely changed and, theoretically at least, a patient with proper treatment should live for his normal span of life or die of some unrelated condition. Certainly the prognosis is much more promising, as indicated by the statistics of the Metropolitan Life Insurance Company which show that the disease is now responsible for about 7000 fewer deaths a year in the United States than it was 20 years ago and that there has been a decrease of 80 per cent in the death rate as a result of the modern treatment at the ages of 45 to 75 years where the mortality of the disease is concentrated. With additional improvement in specific medications and their methods of administration, constant betterment in the outlook of patients with this disease is to be anticipated.

The most important factors in the prognosis are the effectiveness with which the antipernicious anemia medication is given, the state of the nervous system, the occurrence of infections, and the fact that an increased dosage is required in older patients or those with arteriosclerotic changes. The most common cause for failure is the unnecessary and regrettable tendency of the patient to become lax in taking treatment. Usually the ensuing relapse is not complete but it may be of such an extent that the neurologic lesions progress to an irreversible state. It is of first importance in combating this to prescribe an amount of medication which is somewhat in excess of the minimal dosage necessary to keep the blood within normal limits and to insist that each patient report at least every three months for a complete blood examination.

The nervous system involvement has been

minor) or supply the extra dosage some patients need as they grow older (3) inadequacy of the average dose for the individual patient and (4) development of sensitivity to the therapeutic agent (this occurs in a small but important group of the patients)

To prevent therapeutic failure the patient's blood should be examined regularly as a guide to the amount of medication necessary to maintain the blood in normal condition If an infection develops even one of a mild upper respiratory type the dose should be doubled until the infection has entirely subsided For any patient the possibility that a greater dosage is required with increasing age should be kept in mind

Indications of sensitivity to liver extract are flushing of the face palpitation and tachycardia itching of the skin urticaria stuffiness of the nasal passages occasional frank asthmatic attacks and (though rarely) loss of consciousness The immediate symptoms are usually relieved by the subcutaneous injection of 0 5 cc of 1/1000 solution of epinephrin hydrochloride The simplest permanent solution of this problem is to change the therapy to vitamin $B_1$ which can usually be given with impunity Recently however Young Ulrich and Fouts have reported the case of a patient who showed severe allergic symptoms after the injection of vitamin $B_{12}$ concentrate but did not o react to crystalline vitamin $B_1$ If it is desirable to desensitize the patient to liver extract this may be done by injecting subcutaneously from 0 01 cc to 0 05 cc of a solution containing 15 units per cc and doubling the quantity every half hour until a dose of 1 cc is given Oral liver extract or desiccated stomach or liver stomach preparations for oral use may be employed but they are less effective Since folic acid may harm the nervous system it is not recommended that it be employed

If vitamin $B_{12}$ is used it should be given the patient when he is in relapse The dosage follows 10 micrograms of the crystalline form or 15 U S P units of the concentrate daily for the first week the same amount three times weekly for the second and third weeks and twice weekly thereafter until the blood is normal A maintenance dose is 20 micrograms of the crystalline form or 1 cc containing 15 U S P units of the concentrate given every two weeks Further experience will probably indicate that doubling this dosage and giving it every four weeks will maintain the blood in a normal condition

Though 1 microgram daily may suffice for some patients it is inadequate for others The only safe course to pursue is to examine the blood at intervals to determine accurately whether the dose administered is optimal As much as two single doses of 1000 micrograms each have been given intramuscularly 13 weeks apart to a patient with pernicious anemia and subacute combined degeneration Apparently they caused no ill effects, and improvement in the neurologic manifestations appeared to be more rapid than is usually observed when other methods of treatment are used (Bortz 1950) Further experience with this method of treatment is desirable before it can be recommended for general use

When vitamin $B_{12}$ is administered orally even in doses as great as 250 milligrams the therapeutic results are uncertain It has been shown (Bethell Hall and associates) that the activity of vitamin $B_{12}$ when given orally may be greatly increased if combined with extracts of hog s stomach and duodenum Such preparations are not yet available commercially but they may prove practical for oral treatment in the future

*Folic acid should not be employed in the treatment of patients with pernicious anemia* mainly because it is ineffective in controlling the degenerative lesions in the nervous system in fact some claim that it actually causes a progression of these lesions When folic acid is given orally in doses of 5 milligrams daily it is an unsatisfactory form of maintenance treatment Long term evaluation has shown that a high percentage of the patients will suffer a hematologic or neurologic relapse Larger doses though they should maintain the blood in a normal condition are not advisable for the hazard of neurologic relapse is too great The administration of folic acid to normal persons or patients with anemia other than pernicious anemia does not result in alterations in the nervous system Adverse changes are

cytes which are usually 1 per cent or less in relapse The reticulocyte response is in the form of a curve beginning from two to six days after initiation of treatment reaching a peak between the seventh and ninth days and returning to normal by the fifteenth day The height of the curve varies inversely with the level of the red blood cell count before treatment for example if the count is 1 0 million per cubic millimeter the reticulocyte peak would be about 37 per cent 2 0 million per cubic millimeter, 19 per cent, 3 0 million 6 4 per cent, 3 5 million, 1 8 per cent The average increase in the red blood cell count in the first two weeks of treatment varies from about 200 000 to 400,000 per cubic millimeter per week

A patient treated in accordance with the above directions should do well There are however several possible causes for failure (1) relapse due to lack of co-operation by the patient the most common cause of inefficient treatment, (2) failure to double therapeutic dosage in case of infection (even if only

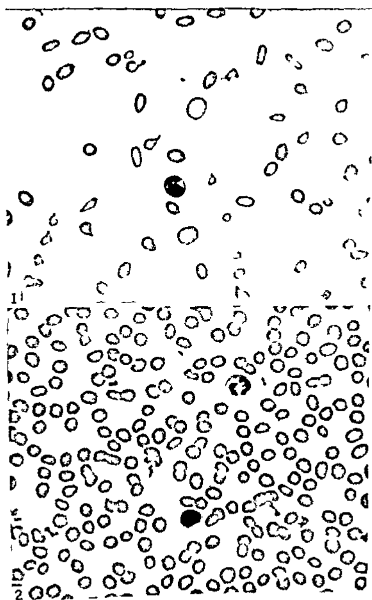



Fig 185 —Change in red cells with specific liver therapy (1) The macrocytosis poikilocytosis and anisocytosis characteristic of pernicious anemia (2) disappeared entirely with adequate treatment (Haden s Principles of Hematology )

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REFERENCES

CASTLE, W. B.: Present Status of the Etiology of Pernicious Anemia. Ann. Int. Med., 1951, *34*, 1093.

JACOBSON, B. M.: The Treatment of Pernicious Anemia. M. Clin. North America, 1949, *33*, 1385.

JONES, F., TILLMAN, C. C. and DARBY, W. J.: Observations on Relapses in Pernicious Anemia. Ann. Int. Med., 1949, *30*, 374.

MECHAM, G. C., VIGNOS, P. J., REINLE, R. W., WEISBERGER, A. S. and EPSTEIN, M.: Vitamin $B_{12}$ Concentrate in the Maintenance of Pernicious Anemia. J. Lab. and Clin. Med., 1950, *35*, 713.

SCHWARTZ, S. O., KAPLAN, S. R. and ARMSTRONG, B. E.: The Long Term Evaluation of Folic Acid in the Treatment of Pernicious Anemia. J. Lab. and Clin. Med., 1950, *35*, 894.

SMITH E L Crystalline Anti Pernicious Anemia Factor Brit M J 1949 2 1367
STEVENS J F and HALL B E Present Day Concepts of Therapy in Pernicious Anemia A Review M Clin North America 1948 32 1113
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STURGIS C C An Analysis of the Causes of Death in One Hundred and Fifty Fatal Cases of Pernicious Anemia Observed since 1927 Tr A Am Physicians 1939 54 46
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## HEMOLYTIC ANEMIA

By RUSSELL L HADEN M D

A hemolytic anemia is one due to a more rapid destruction of erythrocytes than the bone marrow can replace Normally a close balance is maintained between red cell formation and loss If hemolysis is excessive from any cause anemia results

Every normal red blood cell wears out after circulating on the average for 120 days It is removed by reticulo-endothelial cells mostly in the spleen The stroma disintegrates the hemoglobin is split up the iron is set free and bilirubin is formed The bilirubin is bound to protein and tends to remain in the plasma hence the amount of bilirubin present is an indirect measure of the rate of red cell destruction

With excessive loss of erythrocytes the bone marrow attempts to compensate by a higher rate of delivery of cells The bone marrow on examination is hyperplastic with an excessive number of young red cells Since many of the circulating red cells are young they appear as reticulocytes The reticulocyte count is a measure of the rate at which new cells are delivered from the bone marrow An elevated reticulocyte count in the peripheral blood is thus typical of a hemolytic anemia with active marrow

The spleen is overactive in removing abnormal and dying cells from the circulation it is usually enlarged in a hemolytic anemia

Clinically, one sees jaundice and an enlarged spleen in hemolytic anemia In the laboratory one finds a reduction in red cells and hemoglobin an increased reticulocyte count and an increased bilirubin content in the plasma The bone marrow shows excessive erythropoiesis with many normoblasts and erythroblasts

Accelerated hemolysis may be due to agents toxic for the erythrocyte in the blood plasma such as

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3) Chemical poisons such as phenylhydrazine Many other chemical substances will actively destroy red cells—among these are bile salts saponin and snake venoms Intracellular parasites such as those of malaria obviously damage cells in which they are contained

Increased hemolysis may also result from the abnormal shape of a red cell or a qualitative defect in the stroma In hereditary spherocytosis (familial hemolytic jaundice) the basis for the rapid red-cell destruction seems to be the shape (spheroidal) of the erythrocyte Both Mediterranean anemia (Cooley s anemia) and sickle cell anemia stem from a hereditary defect in the stroma or hemoglobin this accelerates hemolysis and produces a hemolytic anemia Rarely abnormal hemolysis seems to be due to a perverted activity of the reticulo-endothelial cells especially in the spleen

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II Increased hemolysis due to excessive removal of red cells abnormal at birth

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REFERENCES

Castle W B Present Status of the Etiology of Pernicious Anemia Ann Int Med 1951 *34* 1093

Jacobson B M The Treatment of Pernicious Anemia M Clin North America 1949 *33* 1385

Jones E Tillman C C and Darby W J Observations on Relapses in Pernicious Anemia Ann Int Med 1949 *30* 374

Mecham G C Vignos P J Reinle R W Weisberger A S and Epstein M Vitamin $B_{12}$ Concentrate in the Maintenance of Pernicious Anemia J Lab and Clin Med 1950 *35* 713

Schwartz S O Kaplan S R and Armstrong B E The Long Term Evaluation of Folic Acid in the Treatment of Pernicious Anemia J Lab and Clin Med 1950 *35* 894

Smith E I Crystalline Anti Pernicious Anemia Factor Brit M J 1949 2 1367
Stevens J E and Hall B E Present Day Concepts of Therapy in Pernicious Anemia A Review M Clin North America 1948 32 1113
Strauss M B Solomon P and Fox H J Y Combined Degeneration of Spinal Cord in Pernicious Anemia Results of Seven Years Experience With Parenteral Liver Therapy New England J Med 1940 222 373
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   4) parasites (as in malaria)

II Increased hemolysis due to excessive removal of red cells abnormal at birth

1) spherocytic anemia (familial hemolytic jaundice),
2) sickle cell anemia,
3) oval cell anemia,
4) Mediterranean anemia (Cooley's anemia)

III Increased hemolysis of undetermined cause (immune hemolysins, overactivity of spleen and other parts of reticulo-endothelial system qualitative defect in stroma or hemoglobin, etc)

The complete clinical and laboratory picture of a hemolytic anemia from any cause is as follows jaundice due to increased bilirubin content of the plasma reduction in red cells and hemoglobin increase in reticulocytes enlargement of the spleen and erythrocyte hyperplasia in the marrow The differential diagnosis depends also on a careful clinical and laboratory study In all hemolytic anemias the size and shape of the red cell should be determined In hereditary spherocytosis the red cells show decreased diameter and increased thickness with increased fragility in hypotonic salt solution in sickle cell anemia the cells become sickle-shaped under aerobic conditions in Cooley s anemia there are numerous target cells usually an increase in the number of nucleated cells and decreased fragility of the red cells in hypotonic salt solutions In all hemolytic anemias, there is reticulocytosis of varying degree in the peripheral blood and the bone marrow constantly shows erythroid hyperplasia

A Coombs antiglobulin test should be made in all cases of hemolytic anemia This test detects antibodies which may be responsible for hemolysins in acquired hemolytic anemia Antiglobulin serum made by injecting a rabbit with normal human serum is mixed with washed red cells from hemolytic anemia Clumping of the red cells indicates a positive reaction to the test

## HEREDITARY SPHEROCYTOSIS

*Synonyms* —Congenital hemolytic jaundice, chronic acholuric jaundice familial hemolytic jaundice

*Definition* —Hereditary spherocytosis is a chronic hemolytic anemia characterized by nonobstructive jaundice, spherocytosis increased hypotonic fragility of the red cells reticulocytosis and splenomegaly There may be hemolytic crises

*Etiology* —It is accepted that spherocytosis or a change in the shape of the erythrocytes from biconcave (normal) to spherical or at least an increase in the thickness of the erythrocytes is a constant finding in the disease

Furthermore it is agreed that this alteration in shape accounts for the increased fragility of the cells as it is the first stage of hemolysis As I have written on another occasion The more spherocytic the cell the nearer it is to the hemolysis point When such an alteration exists the reticulo endothelial cells of the spleen and other organs remove the abnormal cells from the circulation at a more rapid rate than erythrocytes can be produced in the marrow, the result is an anemia The immediate cause, therefore, of the anemia is hyperactivity of the spleen but it should be emphasized that the spherocytosis which is the fundamental fault persists after splenectomy

All the major clinical manifestations of the disease are due to the excessive red cell destruction The jaundice is associated with increased production of bile pigment the splenomegaly results from the augmented activity of the spleen in removing erythrocytes from the circulation the reticulocytosis is evidence of the accelerated production and delivery of red cells

There are two views concerning the cause of the spherocytosis and the increased fragility of the erythrocytes One is that the inherited defect is the abnormal shape of the cells and that the immediate cause of the anemia is the hyperactivity of the spleen with rapid removal of many of these cells from the circulation The other view is that these changes are not inborn errors of erythrocyte formation but are the effect of extrinsic agents acting on the cell during its life in the blood stream According to this theory the spherocytosis, increased erythrocyte fragility reticulocytosis and response to splenectomy are not pathognomonic of congenital hemolytic anemia but may also characterize the acquired type of

the anemia and be produced experimentally Such changes are attributed to the effects of a lytic agent on the normal mature red cells

The victim of the disease often has a history of the disease in several previous generations of his family but the condition may have been so mild in some of his predecessors as to go unrecognized Spherocytosis is transmitted by the two sexes as a Mendelian dominant trait and occurs with equal frequency in both adult life although they may be so mild as to be overlooked For this reason it cannot be said that other cases do not exist in a patient's family unless the patient s relatives have been examined The jaundice is usually very slight except during crisis It has often been said that the patients are "more yellow than sick" as no other complaints may be present The crisis of the disease to which any patient is liable are characterized by fever malaise abdominal pain nausea and vomiting intensification of the jaundice and

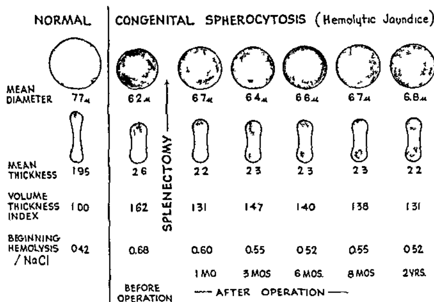



FIG 186 —Chart to show the shape of cells in patient with congenital hemolytic jaundice and effect of splenectomy (Haden s Principles of Hematology )

*Pathology* —There is marked congestion of the spleen which involves the pulp but not the sinuses the organ is enlarged often weighing from 1000 to 1500 grams Ordinarily it is not adherent, in contrast to the spleen in Banti s disease and is easily removed The endothelial cells of the spleen liver bone marrow, and lymph nodes (reticulo-endothelial system) show evidence of activity as indicated by phagocytosis of red blood cells and pigment The liver kidneys and lymph glands have the changes of hemosiderosis Gallstones composed largely of bilirubin are frequently found

*Symptoms and Signs* —Evidences of the disease usually appear in childhood or young a rapid fall in the red blood cell count Cholelithiasis due to increased formation of bile pigments is frequently present Leg ulcers may occur but are uncommon The spleen is palpable in about 75 per cent of the patients but is seldom greatly enlarged it is not common to observe a liver which is significantly increased in size—indeed gross hepatomegaly casts considerable suspicion on the diagnosis Developmental anomalies may occur especially the tower skull ( turmschadel ) A number of others have been reported such as prominent eyes an abnormally wide root of the nose and changes in the teeth On roentgen examination the frontal and

parietal bones may show thickening and striations.

The diagnosis is certain in the presence of hemolytic anemia of familial origin, reticulocytosis, spherocytosis, increased fragility of the erythrocytes, splenomegaly, and nonobstructive jaundice.

*Blood Examination.*—There is commonly a red blood cell count which varies between 2,000,000 and 3,500,000 per c.mm.; the average hemoglobin reading is between 40 and 70 per cent. The color index is most frequently about 1. During spontaneous remissions the red cell count may be normal, whereas in crises it may fall to 1,000,000 per c.mm. or less. The average volume of the cells is somewhat decreased, most commonly varying between 75 and 85 cubic microns, although it may be normal or even increased. The mean erythrocyte diameter is reduced, measuring between 6.2 and 7 microns. The increased thickness of the cells, averaging 2.2 to 3.4 microns instead of the normal of 2 microns or less, is due to the diminished mean cell diameter in association with a normal or only slightly reduced mean corpuscular volume. There is some anisocytosis, but poikilocytosis is not common. Nucleated red blood cells and polychromatophilic cells are frequently present. Ordinarily there are no important changes in the leukocytes or platelets, but in crises the former may be increased. The reticulocytes frequently reach a level between 10 and 15 per cent, and in some patients there may be a very much greater increase. There is usually a decreased resistance of the red blood cells in hypotonic salt solution. Normal red blood cells show hemolysis which begins at 0.44 to 0.48 per cent and is complete at 0.3. In hemolytic jaundice hemolysis may begin at 0.51 to 0.72 per cent and be complete at 0.4 per cent.

The bone marrow shows evidence of increased erythropoietic activity as indicated by hyperplasia of the normoblastic type. These cells make up from 25 to 50 per cent of all nucleated cells; mitosis is common.

*Prognosis and Course of the Disease.*—Victims of spherocytosis often live for years without serious symptoms and may even reach an advanced age. It is characteristic, however, for exacerbations of symptoms to occur, the so-called "crises," at which times persistent vomiting, fever, and abdominal pain occur. Intensification of the jaundice and rapid development of a severe anemia also occur. One of the more distressing complications is the frequently associated cholelithiasis, which results in typical attacks of biliary colic.

*Treatment and Prognosis.*—Splenectomy removes all signs and symptoms of the congenital hemolytic jaundice except spherocytosis. As soon as the diagnosis is proved splenectomy should be performed. The anemia is variable, but even with a mild anemia beginning in childhood the patient is seldom well, growth is often retarded, and resistance to infection is low. It is best to do the splenectomy early. The mortality from operation is almost nil since the spleen is seldom very large and almost never shows adhesions. Infants less than a year old stand the operation well.

Even in mild cases, if splenectomy is not performed, gallstones frequently develop. These in turn may cause colic or lead to cholecystitis.

After splenectomy the jaundice should disappear, and the bilirubin content of the plasma should return to normal and the reticulocyte count become less than 1 per cent within 10 days. Spherocytosis persists. If the operation is not successful, the presence of accessory spleens should be suspected or the possibility of an incorrect diagnosis should be considered. There is usually a rapid rise in the red cells and the hemoglobin. Transfusions are seldom necessary and are best avoided. The usual therapeutic agents, such as iron, arsenic, liver and liver substitutes, are of no value.

REFERENCES

HADEN, R. L.: Hemolytic Anemia. Jour. Lab. and Clin. Med., 1940, 26, 65.

———: Splenectomy in Hemolytic Jaundice. Surg. Clinic. N. Am., 1941, 21, 1453.

ISRAELS, M. C. G., and WILKINSON, J. F.: Hemolytic (Spherocytic) Jaundice in the Adult. Quart. Journal Med., 1938, 7, 137.

THOMPSON, W. I.: Hemolytic Jaundice. Bul. New York Acad. Med., 1939, 15, 174.

TILESON, W.: Hemolytic Jaundice. Medicine, 1932, 1, 355.

## OVALOCYTOSIS

In ovalocytosis, a hereditary blood anomaly transmitted by either sex possibly as a Mendelian dominant trait from 50 to 90 per cent of all circulating erythrocytes may be oval or elliptical in shape The condition is not limited to any race It bears no relationship to "sickling" as no alteration in the shape of these cells occurs in sealed fresh blood preparations Persons with such cells usually do not have an anemia or evidence of excessive red blood-cell destruction It is stated that the mean corpuscular volume may be reduced In such cases the hematocrit reading may be normal if the red cell count is increased above normal

## SICKLE CELL ANEMIA

*Synonyms* —Sicklocytosis meniscocytosis drepanocytic anemia Herrick s syndrome

*Definition* —Sickle cell anemia is a chronic hereditary and familial hemolytic anemia confined with few exceptions to negroes It is due to an intrinsic defect in the erythrocytes and is characterized by the appearance of a considerable number of sickle shaped red cells in the circulating blood the symptoms of an anemia recurrent leg ulcers cardiovascular manifestations and episodes of abdominal pain slight jaundice nausea and vomiting

*Etiology and Pathology* —The disease probably exists from birth as it is usually seen in children although it is observed at all ages It is probably transmitted as a Mendelian dominant characteristic The condition is characterized by periods of activity and quiescence About 7 per cent of all negroe have the sickle cell trait although evidence of anemia appears in only 1 in 40 whose red cells sickle It is generally agreed that sickling is due to a hereditary defect and that the change in shape is an inherent property of the erythrocytes Recently Pauling Itano Singer and Wells have suggested that the hemoglobin in sickle cell anemia has a molecular structure that may be responsible for the shape of the cell Persons with the trait show no characteristic cells on the stained smear but such cells will usually appear in a sealed preparation made from blood obtained from the finger in which stasis has been produced by constriction with a rubber band for five minutes The difference between sickle cell anemia and the sickle cell trait is not clear it may be only that in the anemia the erythrocytes have a greater tendency to undergo changes in shape The explanation of the hemolysis and of the periodic attacks in which it is excessive, is unknown At necropsy fatty degenerative changes and hemosiderosis are found The bone marrow is hyperplastic and contains many nucleated red cells chiefly normoblasts it does not differ from the marrow observed in any type of hemolytic anemia except for the presence of sickle cells Throughout the body but especially in the spleen there are evidences of thrombosis infarction necrosis and hemorrhage The spleen, enlarged and congested in the earlier stage of the disease becomes fibrotic and very small According to Rich the characteristic microscopic findings in this organ are malformation of the splenic sinuses in the immediate vicinity of the Malpighian follicles and collections of pools of blood in fibrosed and atrophic areas The small and medium sized arteries may have thickened walls and show proliferation of the intimal cells Thrombosis of small vessels may cause lesions of the nervous system

*Symptoms* —Even with a moderately advanced anemia the patient may be free from symptoms except for quickness of fatigue Commonly however the patient complains of anemia and a slight jaundice The active symptoms of the disease are attacks of abdominal pain nausea vomiting and moderate jaundice Sometimes the pain may be sharp and this with the associated fever nausea and vomiting and leukocytosis suggests an acute condition requiring surgery Additional symptoms are headache malaise and pain in the muscles and joints symptoms usually associated with a moderate febrile reaction Remarkable features of the disease are the leg ulcers and the cardiac involvement Characteristically the ulcers occur about the ankles average 1 to 3 cm in diameter and have sharp edges with a "punched-out" appearance like luetic ulcers In a fair pro

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## REFERENCES

Haden R L Hemolytic Anemia Jour Lab and Clin Med 1940 *26* 65

——— Splenectomy in Hemolytic Jaundice Surg Clinic N Am 1941 *21* 1453

Israels M C G and Wilkinson J F Hemolytic (Spherocytic) Jaundice in the Adult Quart Journal Med 1938 *7* 137

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portion of the patients, there is definite cardiac hypertrophy, not infrequently there are symptoms of chronic cardiac failure A history of recurrent attacks of painful joints in a young person with an enlarged heart and an apical systolic murmur, sometimes leads to an incorrect diagnosis of rheumatic mitral insufficiency Early in sickle cell anemia, the spleen and liver become moderately enlarged Roentgenographic changes occur in the skull and other bones The earliest change in the skull is a "ground glass" appearance and a peculiar radial striation ("hair on end") is seen Neurologic manifestations due to thrombosis are common, they include hemiplegia, aphasia headache convulsions, meningeal symptoms cranial nerve palsies, and paresthesia of the extremities

*Laboratory Findings* —Commonly, a red-blood cell count varying between 1,000 000 and 2 000,000 per c mm is found and with




Fig 187 —Above blood in sickle cell anemia photomicrograph of blood of patient with sickle cell anemia Note the oat and sickle-shaped cells and numerous cells with an elevation in the center Below photomicrograph of blood of same patient after standing several hours under sealed cover glass (Haden courtesy of Arch Int Med)

this there is a corresponding reduction in the hemoglobin hence the color index is normal The anemia is most frequently of the normocytic variety but it may be either macrocytic or microcytic The characteristic findings are the sickle cells These may be seen on a stained smear but are observed to best advantage on a sealed wet-film preparation that has stood for six or more hours Nucleated red cells are usually numerous and the reticulocytes as a rule, average between 5 and 25 per cent The blood bilirubin is frequently increased to from 1 to 3 mg per 100 cc of blood the icterus index varies between 15 to 25 units There is commonly a leukocytosis of from 12 000 to 30 000 per c mm and the platelets are moderately increased

*Treatment and Prognosis* —No specific remedy for sickle cell anemia is known but blood transfusions may induce a remission that lasts for several months but severe reactions may follow the transfusions Liver, ventriculin and iron are ineffective against the anemia The only therapy indicated is general hygienic measures treatment of cardiac failure if present by the usual measures and local treatment of the leg ulcers There is no convincing evidence that splenectomy is beneficial although this has been tried in a few cases The patients are often underdeveloped and emaciated Exacerbations of the disease may be prolonged and frequent and seriously handicap the patient On the other hand, there may be long latent periods during which the patient suffers but slight inconvenience from the disease In general however sickle cell anemia must be regarded as a serious condition which may ultimately result in death although it is not incompatible with survival to an advanced age The sickle cell trait is symptomless and is of no importance to the individual except insofar as it may be transmitted to his offspring

REFERENCES


Diggs L W and Pettit V D A Comparison of Methods Used in the Detection of the Sickle Cell Trait Jour Lab and Clin Med 1940 25 1106

Herrick J B Peculiar Elongated and Sickle-shaped Red Corpuscles in a Case of Severe Anemia Arch Int Med 1910 6 517

Steinberg Bernard Sickle-Cell Anemia Arch Path 1930 9 877

Tomlinson W J Studies of Sicklemia Blood With a New Method for its Rapid Diagnosis Am Jour Clin Path 1941 11 835

Winsor T and Burch G E Diagnostic Physicochemical Blood Tests in Sickle Cell Anemia Am Jour Med Sci 1944 207 152

Pauling Linus Itona Harvey A Singer S J and Wells Ibert C Sickle-Cell Anemia A Molecular Disease Science 1949 110 543


## MEDITERRANEAN ANEMIA

*Synonyms* —Cooley s anemia thallassemia erythroblastic anemia

*Definition* —Mediterranean anemia is a chronic microcytic hypochromic anemia It is often familial probably always hereditary, and limited largely to those of Greek Italian and Sicilian parentage It is characterized by many immature red cells in the peripheral blood, erythroid hyperplasia of the bone marrow flattened erythrocytes with many target cells showing decreased hypotonic fragility and typical x ray changes in the bones

*Etiology* —It seems evident that Mediterranean anemia stems from an inherited defect in the red cell which makes it more susceptible to hemolysis hence the laboratory findings reflect expressions of this defect *plus those of a hemolytic anemia* The defective red cells live only a short time Hemolysis is excessive, as shown by the anemia and increased icterus index The bone marrow as in other hemolytic anemias attempts to compensate for the increased cell loss hence there is erythroid hyperplasia with the appearance of an increased number of reticulocytes and nucleated cells in the peripheral blood

At autopsy abundant depositions of iron are found in the tissues The spleen is usually very large with infarcts and adhesions The bone marrow is hyperplastic There is a proliferation of new bone with a thickening of the calvarium that results in the radial arrangement of bone spicules which gives the so-called hair-on-end' radiograph

*Symptoms and Signs* —The onset of the disease is gradual but the anemia usually

portion of the patients there is definite cardiac hypertrophy not infrequently, there are symptoms of chronic cardiac failure A history of recurrent attacks of painful joints in a young person with an enlarged heart and an apical systolic murmur sometimes leads to an incorrect diagnosis of rheumatic mitral insufficiency Early in sickle cell anemia, the spleen and liver become moderately enlarged Roentgenographic changes occur in the skull and other bones The earliest change in the skull is a "ground glass" appearance and a peculiar radial striation ("hair on end") is seen Neurologic manifestations due to thrombosis are common they include hemiplegia, aphasia, headache convulsions, meningeal symptoms, cranial nerve palsies, and paresthesia of the extremities

*Laboratory Findings* —Commonly, a red blood cell count varying between 1 000,000 and 2 000 000 per c mm is found and, with

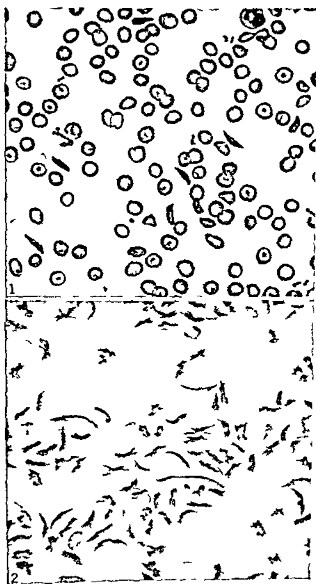



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first child affected the symptoms may be mild. These usually become more severe in the children of succeeding pregnancies. As the symptoms are accelerated, intra-uterine death often occurs.

*Blood.*—The anemia is macrocytic and usually severe, the red cell count being in the neighborhood of one million. Large numbers of nucleated red cells are present. There is usually leukocytosis. The nucleated erythrocytes are of all types, but with survival of the child these disappear in a few days.

*Treatment.*—If not dead at birth, the child is likely to die within a week. Supportive measures should be instituted at once. Blood transfusions from an Rh negative donor—and preferably from one that is also a group-O donor—should be given intravenously. If a mother has previously given birth to a child with erythroblastosis she will usually exhibit a rising anti-Rh titer late in her current pregnancy. If this is found, it is best to induce labor to forestall the continuing hemolysis. Exsanguination of the newborn child and replacement with Rh negative group-O blood may be necessary.

## ANEMIA IN PREGNANCY

By Frank H. Bethell, M.D.

Anemia is a common accompaniment of pregnancy and is usually due to preexisting deficiency of substances required for normal red cell production and hemoglobin synthesis. However, the lowering of erythrocyte values which occurs almost uniformly during gestation does not necessarily constitute anemia. It is accounted for by increased plasma volume and is therefore a state of hydremia rather than true anemia.

The significance of anemia in pregnancy gains weight from the fact that the fetal requirements for blood formation must be supplied by the mother. Although a great many substances are utilized in the formation of blood cells, the deficiencies most likely to occur are of iron, protein and certain fractions of the vitamin B complex. The immediate needs of the fetus in the manufacture of red blood cells are adequately met even when there is a severe deficiency in the mother, although this entails still further depletion of her own materials. On the other hand, the reserves normally stored for use in the first months of extra-uterine life are supplied scarcely if at all in the presence of such deficiency. This division of scanty essential materials between mother and fetus has been shown to be true in the case of iron, and it probably also holds for other constituents of the blood cells.

Anemia in pregnancy may be entirely coincidental, as illustrated by persons with various disorders affecting the blood or blood forming organs. But in such cases the added demands of pregnancy materially increase the disability caused by the original condition. Thus women suffering from leukemia, aplastic anemia, untreated pernicious anemia or certain hemolytic anemias tolerate gestation poorly and frequently fail to secure a viable child.

In the great majority of cases of anemia occurring during pregnancy, the condition is attributable to the gravid state. Yet the preexisting health of the pregnant woman, and especially her nutritional status with respect to the substances mentioned above, largely determine whether or not the added demands of gestation will result in anemia.

Before the incidence of anemia in pregnancy can be discussed, a normal range of values must be defined. It is the lack of universally accepted standards of normality which has made difficult or impossible a comparison of the data supplied in many reported series of cases. Standards based on the examination of subjects assumed to be healthy because free from apparent disease are too low when compared with values obtained for persons who meet rigid physical and nutritional requirements. Quantitatively the difference is not great, but anemia of slight degree should be regarded less as a cause of disability than as an indication of suboptimum health, often dependent upon nutritional inadequacy. Erythrocyte and hemoglobin values reach their lowest points during the sixth or seventh month of gestation. Red blood cell counts of less than 3,700,000 per cu. mm. and hemoglobin values below 11 grams per 100 cc. observed at any time during pregnancy

appears during the first two years of life The first symptoms are pallor and enlarged spleen The disease progresses slowly the anemia increases, the spleen grows larger, and growth is retarded A mongoloid cast of countenance is frequently found among the victims of the condition As the disease continues the spleen often becomes immense and the anemia extreme and there is usually some enlargement of the liver

The typical roentgenographic signs are not always present but are striking when they are when these signs are well established there is a diploic space with vertical striations at right angles to the inner tables

*Blood* —Early in the disease there are few distinctive features and only a mild anemia The typical large number of normoblasts appears later The anemia is microcytic and hypochromic The red cell count is usually between 2 and 3 millions per cubic millimeter and the hemoglobin measures between 20 and 30 per cent The reticulocytes are increased (5 10 per cent) and, with progression there are diffuse basophilia poikilocytosis, and anisocytosis Macrocytes are common although the mean cell volume is small A target cell shows a deeply stained center a clear area and a deeply stained periphery The macrocytes often show irregularly distributed hemoglobin 'Target cells are looked on as characteristic of Mediterranean anemia but are also seen in other conditions such as sickle cell anemia and obstructive jaundice

The presence of nucleated red blood cells as typical and immature normoblasts and microblasts is characteristic of advanced disease

The leukocytes are usually increased in number, varying between 10 000 and 25 000 per cubic millimeter Immature white cells may appear

The red cells show decreased hypotonic fragility, as one would expect since the cell thickness is decreased

The icterus index is typically elevated

*Treatment* —The treatment of Cooley s anemia is purely symptomatic since the hereditary defect is not influenced It differs from other forms of microcytic anemia in that it does not respond to iron therapy Liver and drugs produce no effect Blood transfusion is palliative only

*Prognosis and Course* —If the disease occurs early in the patient s life, it gradually progresses to death Survival to adulthood is rare but is more common than previously thought It is recognized, however, that mild cases do exist In these the progress of the disease is so slow that it may not be recognized till the victim is an adult A carrier state in adults is also recognized

## ERYTHROBLASTOSIS FETALIS

*Synonyms* —Erythroblastosis neonatorum hydrops fetalis congenital anemia of the newborn icterus gravis

*Definition* —Three serious diseases of the newborn, icterus gravis congenital anemia of the newborn and hydrops fetalis are included in the general term *erythroblastosis fetalis* This erythroblastosis is characterized by excessive hemolysis and abnormal erythropoiesis

The three diseases have three conditions in common anemia with many erythroblasts enlargement of both spleen and liver and extra medullary formation of blood cells

*Etiology* —The disease is primarily an abnormal hemolysis due to isoimmunization of an Rh negative mother by an Rh positive fetus Immune bodies in the blood of the mother increase in intensity with each Rh-positive child hence manifestation of the condition becomes more severe in each child The early evidence of the condition is anemia with more prolonged and intense immunization fetal hydrops develops

*Pathology* —Intense yellow-staining of all the body tissues and enlargement of both liver and spleen are the principal pathological features of the disease The bone marrow shows active hematopoiesis Extramedullary hematopoiesis is striking

*Symptoms and Signs* —The classic symptoms of the disease are jaundice soon after birth with a rapid development of anemia In infants most severely affected edema also develops early There is a great variation in the combination of jaundice anemia, and hydrops The blood shows many nucleated erythrocytes With a mother s

first child affected the symptoms may be mild These usually become more severe in the children of succeeding pregnancies As the symptoms are accelerated intrauterine death often occurs

*Blood* — The anemia is macrocytic and usually severe, the red-cell count being in the neighborhood of one million Large numbers of nucleated red cells are present There is usually leukocytosis The nucleated erythrocytes are of all types but with survival of the child these disappear in a few days

*Treatment* —If not dead at birth the child is likely to die within a week Supportive measures should be instituted at once Blood transfusions from an Rh negative donor—and preferably from one that is also a group-O donor—should be given intravenously If a mother has previously given birth to a child with erythroblastosis she will usually exhibit a rising anti Rh titer late in her current pregnancy If this is found it is best to induce labor to forestall the continuing hemolysis Exsanguination of the newborn child and replacement with Rh negative group-O blood may be necessary

## ANEMIA IN PREGNANCY

By Frank H Bethell M D

Anemia is a common accompaniment of pregnancy and is usually due to preexisting deficiency of substances required for normal red-cell production and hemoglobin synthesis However the lowering of erythrocyte values which occurs almost uniformly during gestation does not necessarily constitute anemia It is accounted for by increased plasma volume and is therefore a state of hydremia rather than true anemia

The significance of anemia in pregnancy gains weight from the fact that the fetal requirements for blood formation must be supplied by the mother Although a great many substances are utilized in the formation of blood cells the deficiencies most likely to occur are of iron protein and certain fractions of the vitamin B complex The immediate needs of the fetus in the manufacture of red blood cells are adequately met even when there is a severe deficiency in the mother although this entails still further depletion of her own materials On the other hand the reserves normally stored for use in the first months of extra uterine life are supplied scarcely if at all in the presence of such deficiency This division of scanty essential materials between mother and fetus has been shown to be true in the case of iron and it probably also holds for other constituents of the blood cells

Anemia in pregnancy may be entirely coincidental as illustrated by persons with various disorders affecting the blood or blood forming organs But in such cases the added demands of pregnancy materially increase the disability caused by the original condition Thus women suffering from leukemia aplastic anemia untreated pernicious anemia or certain hemolytic anemias tolerate gestation poorly and frequently fail to secure a viable child

In the great majority of cases of anemia occurring during pregnancy the condition is attributable to the gravid state Yet the preexisting health of the pregnant woman and especially her nutritional status with respect to the substances mentioned above largely determine whether or not the added demands of gestation will result in anemia

Before the incidence of anemia in pregnancy can be discussed a normal range of values must be defined It is the lack of universally accepted standards of normality which has made difficult or impossible a comparison of the data supplied in many reported series of cases Standards based on the examination of subjects assumed to be healthy because free from apparent disease are too low when compared with values obtained for persons who meet rigid physical and nutritional requirements Quantitatively the difference is not great but anemia of slight degree should be regarded less as a cause of disability than as an indication of suboptimum health often dependent upon nutritional inadequacy Erythrocyte and hemoglobin values reach their lowest points during the sixth or seventh month of gestation Red blood cell counts of less than 3 700 000 per cu mm and hemoglobin values below 11 grams per 100 cc observed at any time during pregnancy

should be regarded as probably abnormal although hydremia may, in some instances account for values as low as 3 500,000 red cells and 10 grams of hemoglobin

Among the many causes of anemia affecting both *gravid* and *nongravid* women, specific deficiencies may be regarded as among the most important Their significance is based upon their frequency and their vulnerability to the three chief weapons of disease control prevention, recognition, and correction Since particular deficiencies result in characteristic abnormalities in the blood picture, exact diagnosis and effective treatment require careful hematologic evaluation with particular emphasis upon the size of the red blood cells and the degree to which they are filled with hemoglobin In some cases, bone marrow examination is of great aid in the interpretation of the hemopoietic disturbance and as a guide to therapy

Iron Deficiency Anemia of Pregnancy —Depending upon the nature of the group under observation iron-deficiency anemia occurs in from 15 to 30 per cent of gravid women Fetal requirement for iron is greatest during the last trimester of gestation yet hypochromic anemia if it occurs, *usually manifests itself by the fifth month* of pregnancy *Such anemia is dependent upon iron depletion before the onset of pregnancy,* due most often to low dietary iron intake menstrual abnormalities or previous pregnancies The blood picture characteristic of iron deficiency in pregnancy is hypochromic with a low color index Microcytosis is less conspicuous than in similar anemias occurring in nongravid women

Careful dietary studies have shown that the incidence of hypochromic anemia is extremely low *among pregnant women who* habitually get a diet supplying 16 or more mgm of iron daily The incidence is greatest among those *who received* less than 8 mgm of food iron When iron depletion with anemia is present, correction of the diet will not suffice to restore normal blood values and reliance must be placed on medicinal iron preparations Gastrointestinal intolerance to the more readily ionizable ferrous salts occurs quite *frequently in pregnant* women It can usually be prevented by having the medication taken immediately after meals and by starting with a single daily dose of 0 3 gm of ferrous sulfate and subsequently adding doses until one is taken after each meal Ferrous gluconate is sometimes better tolerated than the sulfate, and there is a colloidal preparation of iron available in capsules (Ferrocol) which is especially well received

Macrocytic Anemia of Pregnancy — It has been common experience that a considerable number of cases of anemia associated with pregnancy fail to respond satisfactorily to iron therapy alone *Evidence has been produced that such anemia* is dependent upon other deficiencies of the diet and that it may be differentiated from simple iron deficiency by a tendency of the circulating red cells to exhibit significant macrocytosis The incidence of macrocytic anemia in pregnancy usually of mild degree has been found in different groups of subjects, to vary between 10 and 20 per cent Dietary studies have revealed a close correlation between the occurrence of such anemia and low intake of protein, especially that derived from animal sources Improvement of the *diet with daily intake of 100 gms or more* of protein of good quality has led to correction of the anemia even if treatment was deferred until the last trimester of gestation

It seems probable that the so-called "pernicious anemia of pregnancy a rare entity represents a more severe and progressive stage of the relatively common milder form of macrocytic anemia Such anemia may respond to a high intake of protein *alone Response to parenteral administration* of refined and concentrated liver extracts is poor and vitamin $B_1$ has been shown to be completely ineffective in the treatment of pernicious anemia of pregnancy *and the puerperium Folic acid on the* other hand produces excellent responses in patients with this disorder Crude parenteral liver extracts in large doses as well as oral preparations of liver are also effective in *the treatment of pernicious* anemia of pregnancy and the puerperium

In summary anemia is frequently associated with pregnancy and is usually due to

long-standing suboptimal nutrition with menstrual abnormalities and previous pregnancies serving as important aggravating factors Correction of anemia in pregnancy requires recognition of the nature of the deficiency which is facilitated by study of the morphologic changes of the circulating red cells and sometimes by bone marrow examination The important therapeutic agents in the management of such anemia are high dietary intake of good quality protein medicinal iron preparations and when severe macrocytic anemia is present folic acid

### REFERENCES


Bethell, F H Gardiner S H and Mackinnon F The Influence of Iron and Diet on the Blood in Pregnancy Ann Int Med 1939 *13* 91

Day L A Hall B E and Pease C L Macrocytic Anemia of Pregnancy Refractory to Vitamin $B_1$ Therapy Response to Treatment with Folic Acid. Proc Staff Meet Mayo Clin 1949 *24* 149


## SIMPLE CHRONIC ANEMIA

By simple chronic anemia is meant normocytic normochromic anemia associated with a wide variety of pathologic conditions These include some cases of chronic infection malignancy nutritional deficiency states endocrine disorders (such as hypothyroidism and Addison s disease) and metabolic disturbances (such as chronic hepatic disease and chronic nephritis with uremia)

The blood picture in simple chronic anemia is nonspecific and treatment except for blood transfusions is dependent upon diagnosis and correction of the primary condition The lowered erythrocytic values are probably due in most instances to a decreased rate of production of red corpuscles and hemoglobin Such anemia should be carefully distinguished from hemolytic myelophthisic and specific nutritional deficiency anemias

## POLYCYTHEMIA

By Russell L Haden M D

*Synonyms* —Erythremia polycythemia rubra vera Vaquez s disease Osler s disease

*Definition* —Polycythemia is an abnormal increase in red blood cells in the circulating blood Since a cell count indicates only the number of cells per unit volume of blood a high count may be due to blood concentration from dehydration Here the increase is only apparent since the total number of cells is unchanged In true polycythemia or erythremia there is an abnormally large mass of red cells per kilogram of body weight This is due to an increase in total blood volume as well as to a greater number of cells per unit volume of blood Erythrocytosis indicates an increased number of red cells without an increase in red-cell mass per kilogram Few men have a red-cell count above 5 500 000 and any count above 6 000 000 is usually abnormal The comparable figures for women are 5 000 000 and 5 500 000 An erythrocytosis is not uncommon in obese plethoric men and women and may also result from the conditions listed below as causative factors in erythremia

Polycythemia vera or erythremia may be due to some chronic interference with oxygenation an interference due (1) to low barometric pressure in high altitudes (2) to a disturbance in pulmonary circulation (as in Ayerza s disease) (3) to a by passing of the lungs in congenital heart disease or (4) to an alteration in blood pigment (as in methemoglobinemia) In all such cases the hemoglobin cannot properly fulfill its function of carrying oxygen so the total amount may be increased to compensate for the decreased oxygen capacity This condition is designated symptomatic or secondary polycythemia vera since there is an evident cause of the increase in red-cell mass per kilogram of body weight Idiopathic polycythemia vera occurs with known cause A classification of polycythemia is summarized in table 61

*Etiology* —Since anoxemia is a known stimulus for red-cell overproduction and is the evident cause of the high red-cell counts found in cases of symptomatic polycythemia vera attempts have been made to explain the idiopathic type on this basis but no such explanation has been proved No disturbance in the gas-exchanging functions

should be regarded as probably abnormal, although hydremia may, in some instances account for values as low as 3 500 000 red cells and 10 grams of hemoglobin

Among the many causes of anemia affecting both gravid and nongravid women, specific deficiencies may be regarded as among the most important Their significance is based upon their frequency and their vulnerability to the three chief weapons of disease control prevention, recognition and correction Since particular deficiencies result in characteristic abnormalities in the blood picture, exact diagnosis and effective treatment require careful hematologic evaluation with particular emphasis upon the size of the red blood cells and the degree to which they are filled with hemoglobin In some cases, bone marrow examination is of great aid in the interpretation of the hemopoietic disturbance and as a guide to therapy

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Nitrogen mustard also gives excellent results in producing remission. The drug is given as for Hodgkin's disease in a course of 0.1 milligram per kilogram of body weight on four consecutive days, but a total dosage over the four-day period should not exceed 24 milligrams.

TABLE 61.—CLASSIFICATION OF POLYCYTHEMIA

1 Erythrocytosis (secondary or simple polycythemia)
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      (1) low barometric pressure
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         b decreased aerating surface due to lung disease
      (3) impaired capacity of hemoglobin to carry oxygen as in methemoglobinemia
   B Idiopathic polycythemia vera of unknown cause

## HEMORRHAGIC DISEASES

By EUGENE L. LOZNER, M.D.

*Definition.*—A hemorrhagic disease may be said to exist whenever a patient shows a tendency to bleed excessively. Such bleeding may occur into or from the skin, into or from the mucous membrane, into a joint space or, in fact, into any part of the body, without any known trauma or with trauma so trivial that the normal individual would have shown little or no evidence of bleeding. In most patients with hemorrhagic disease bleeding occurs at several sites in the body, and there is little doubt that a generalized breakdown in the hemostatic mechanism has taken place. In other patients the bleeding from one source may be particularly prominent, for example, that from the uterine mucosa or that into one joint space. Such patients may be treated by gynecologists or orthopedic surgeons before it is appreciated that the local bleeding is merely a manifestation of a more generalized disorder.

*Pathophysiology and Classification.*—In order to understand satisfactorily the nature of the hemorrhagic diseases it is necessary to appreciate the nature of the normal hemostatic mechanisms. Unfortunately there still remains considerable dispute about the latter. In brief, the body possesses two main defenses against hemorrhage. For want of better terms these may be called the *vascular defense* and the *blood-coagulability defense*. Whenever either of these fails the possibility of hemorrhage exists. Failure of these defenses may occur either because the trauma has overwhelmed them or because they are unequal to even a trivial trauma. It is the latter situation which is most often observed in the hemorrhagic diseases. The vascular defense consists in (1) the ability of blood vessels to maintain their integrity despite increases in intravascular pressure and despite trauma, (2) *their faculty of constriction and retraction* when severed, and (3) the mobilization of platelets to the vascular wound where they agglutinate and cause the retraction of fibrin. The blood-coagulability defense consists in the ability of the blood to clot upon being shed or, expressed in another way, the transformation of fibrinogen catalyzed by *the enzyme thrombin from its soluble* state within the blood vessels to its insoluble state, or gel form (known as fibrin), upon the release of blood from the blood vessels. In the conversion of fibrinogen to fibrin by thrombin at least three other constituents of the plasma play a role: ionized calcium, prothrombin and thromboplastin. The source of the latter material remains controversial. It is defined fundamentally as a physiological complex which catalyzes the conversion of prothrombin to thrombin in the presence of ionized calcium. Thromboplastic activity has been found in many tissues and exists in the plasma itself. It is found in high concentrations in such tissues as lung or brain. Thromboplastin or something very closely allied to it may be present in the platelets. Recent studies have indicated that, in addition to the above-mentioned three constituents of the plasma, other accelerator substances may play a role in the conversion of prothrombin to thrombin. These accelerator substances are present in both plasma and serum. The

of the blood such as occurs in methemoglobinemia, has ever been demonstrated. The possibility of a defect in oxygenation, a defect due to some abnormality in the pulmonary epithelium, has also been suggested but not demonstrated. There is nothing to suggest that the cells live longer than normal. The bone marrow studies show overproduction of red cells.

*Reznikoff, Foot, and Bethea* have emphasized changes in the arteries of the marrow in idiopathic polycythemia vera similar to those seen in thromboangiitis obliterans. Most observers agree that the bone marrow is primarily at fault in the idiopathic type. The characteristic erythroblastic characteristic of polycythemia vera may be analogous to the myeloblastic overactivity seen in chronic myeloid leukemia.

*Pathology.*—With the characteristic increase in blood volume due to the greater number of red blood cells, the veins are distended and the organs engorged. *Varices are common; thromboses are frequent.*

The spleen is enlarged in all advanced cases, but the diagnosis often may be made before splenomegaly occurs. There is hyperplasia of the pulp, mostly with mature red blood cells. The bone marrow is red and shows hyperplasia of all the marrow elements.

*Symptoms and Signs.*—Early in the disease there are few symptoms. The most important are headache, tiredness and vertigo. Cyanosis and splenomegaly are present in most advanced cases. Early in the disease there may be only ruddiness of complexion and the spleen may or may not be enlarged. As the disease progresses real cyanosis develops. But there may be full blown polycythemia vera without changes in the skin.

Vascular complications are common. Venous and arterial thromboses are frequent. These may occur at widely varying locations. Venous varicosities are seen in many patients. Hypertension also frequently occurs. This may not necessarily be due to the disease since most victims of polycythemia vera are middle-aged or older. Many patients develop gout when the disease is well marked. Erythromelalgia may be observed.

*Blood.*—The red cell count, the hematocrit reading, and the hemoglobin determination are always increased in polycythemia. The red cells usually number more than six million. The hematocrit reading is seldom less than 55 cc. per 100 cc. of blood. Red cell counts as high as 10,000,000 may occur. The blood volume is always increased in polycythemia vera; this is due to the increase in red-cell mass. The change in the red cell mass is best indicated by the number of *cubic centimeters of packed red cells per kilogram of body weight*; this number is determined from the blood volume and the hematocrit reading. In the absence of dehydration, *a red cell count of six million or more* with a hematocrit reading of 55 or more is presumptive evidence of polycythemia vera.

Leukocytosis is common and may occur very early in the course of the disease. Later very high counts may be observed. When *the spleen becomes very large and the white* cell count very high, immature white cells, myelocytes and myeloblasts are common. The blood at this stage may suggest myeloid leukemia.

The platelet count may be high and be a factor in thrombosis, especially when the *viscosity of the blood is high.*

*Treatment.*—It is questionable whether symptomatic polycythemia vera should be treated unless the *increase in red cells is so* extreme as to interfere with the circulation. In idiopathic polycythemia vera this does cause embarrassment of the circulation and as it is progressive, treatment should be given. Various hemolytic agents such as phenylhydrazine have been tried but simply produce a hemolytic anemia. The excess of blood may be removed by frequent venesection with the production of an iron deficiency (microcytic) anemia. But it is far better to prevent excessive formation of red cells in the bone marrow. $P_{32}$ gives excellent results but is not generally available. Radioactive phosphorus is given by mouth or by vein in varying amounts and at varying intervals. The action is slow. Similarly, *x*-ray irradiation may be used but the results are less satisfactory than

those obtained with radioactive phosphorus

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material in serum is much the more potent of the two

The exact role of the platelets in blood coagulation and in vascular defense remains poorly understood It is generally agreed that the platelets are important in the retraction of fibrin, once it is formed, and in the general structure of the thrombus which seals a blood vessel It is also agreed that a diminution of platelets is frequently associated with an increase in capillary fragility and an increased tendency to bleed from small wounds Thus there appears to be a positive correlation between platelets and vascular function For this reason, the hemorrhagic diseases in which platelets are reduced may be included in those in which vascular defense has failed

The hemorrhagic diseases may be classified into two groups—those in which vascular defense has failed and those in which blood coagulability defense has failed (Table 61) In the former group there may be a still further subclassification depending upon whether the platelet count is normal or reduced If normal, the term nonthrombocytopenic purpura may be applied When the platelets are reduced the term thrombocytopenic purpura is used

## THROMBOCYTOPENIC PURPURA

*Synonyms* —Werlhof s disease (*see classification below*) purpura hemorrhagica morbus maculosus hemorrhagicus

*Definition* —Thrombocytopenic purpura is a hemorrhagic disease characterized by bleeding into and from the skin and mucous membranes diminished platelets increased capillary fragility, prolonged bleeding time, poor clot retraction and decreased prothrombin consumption

*Etiology and Classification* —There are essentially three types of thrombocytopenic purpura—the idiopathic variety etiology unknown (Werlhof s disease primary thrombocytopenic purpura essential thrombocytopenic purpura) the toxic or allergic variety, in which a drug or antigen can definitely be implicated and the secondary (symptomatic) variety in which the thrombocytopenia is but one manifestation of either a generalized disorder of the bone marrow, (such as leukemia aplastic anemia, pernicious anemia, lymphomatosis, carcinomatosis, or tuberculosis) or a generalized disorder of the spleen producing the syndrome of "hypersplenism (such as Lænnec s cirrhosis, congestive splenomegaly, or Gaucher's disease) Of these varieties, the idiopathic one is probably the least common and secondary thrombocytopenia the most common

## IDIOPATHIC THROMBOCYTOPENIC PURPURA

This disease is most commonly seen in children in whom the incidence as to sex is equal and there is a tendency to spontaneous remission In adults, the incidence ratio females to males, is at least 3 1, suggesting to some an endocrine aspect to the condition

*Pathology and Physiology* —At present, there are two major schools of thought on the pathogenesis of idiopathic thrombocytopenia The first was probably introduced by Frank (1915), who suggested that the spleen inhibited the formation of platelets from the megakaryocytes in the bone marrow The second was suggested by Kaznelson a year later who likening the situation to congenital hemolytic jaundice, postulated that the spleen actually destroyed the platelets and so produced thrombocytopenia The first school is supported to some extent, by the occasional observation that extracts of the spleens of patients with this type of purpura will produce thrombocytopenia when injected into animals The recent studies in congenital thrombocytopenic purpura suggest the placental transfer of a humoral substance, inasmuch as it has been observed that mothers with thrombocytopenic purpura, whether splenectomized or not, usually give birth to babies with transient thrombocytopenia

The findings at autopsy are chiefly those of extensive hemorrhage throughout the body The bone marrow in the usual patient shows the megakaryocytes present in normal or increased numbers Recent studies have indicated that there may also be qualitative changes in the morphology of the megakaryocytes such as the absence of platelet formation The bone marrow may

also be hyperplastic particularly in the erythroid series as the result of acute and chronic blood loss It is of significance in this disorder that the size of the spleen is almost always within normal limits This is in contrast to other cytopenic disorders in which splenomegaly usually prevails

*Symptoms* —The disease varies in both severity and course There may be an acute, rather fulminating course with extensive bleeding from the skin and mucous membranes and with menorrhagia to the point of producing severe anemia and peripheral vascular collapse On the other hand some patients have only mild bruising of the skin moderate purpura and relatively little bleeding from the mucous membranes In the fulminating cases and also unfortunately, in some of the milder cases, cerebral vascular hemorrhage may supervene



Fig 188 —Strongly positive tourniquet test in a case of chronic purpura hemorrhagica Platelet count 40 000 per c mm bleeding time forty two minutes Note that there are few petechiæ in the area compressed by the blood pressure cuff (Wintrobe s Clinical Hematology )

*Signs* —The only signs present are those of the various hemorrhages The uterus may be palpable in instances of severe menorrhagia The spleen is rarely palpable in primary idiopathic thrombocytopenic purpura

*Course of Disease* —The course as indicated above, may vary considerably Approximately a third of the patients will have spontaneous remissions which may be more or less permanent In most of the patients there is a tendency to remission and relapse, and these are rather unpredictable In general there is a greater tendency to spontaneous remission in children and young adults than in the older age groups

*Diagnosis* —The diagnosis of idiopathic thrombocytopenic purpura rests primarily upon the laboratory findings (including those of bone marrow aspiration) and upon the exclusion of known etiologic factors such as chemical and physical agents infectious diseases allergies and the various systemic diseases which involve either the bone marrow or the spleen and may produce secondary thrombocytopenia

*Complications* —There are two complications which must be taken very seriously The first of these as already mentioned is cerebral vascular hemorrhage The second is uterine bleeding which may be excessive It is obvious that this amount of bleeding cannot go on for any length of time without serious consequences

*Laboratory Findings* —The positive findings are a reduction in the number of platelets deficiency in clot retraction a positive tourniquet test (Fig 188), and a prolonged bleeding time Important negative findings are a normal clotting time and a normal prothrombin time

Recent studies have indicated that there is a definite coagulation defect in thrombocytopenic purpura—failure of conversion of the usual amounts of prothrombin to thrombin in the course of coagulation There is sufficient conversion to result in a normal venous clotting time However when coagulation is studied more closely it is

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The exact role of the platelets in blood coagulation and in vascular defense remains poorly understood It is generally agreed that the platelets are important in the retraction of fibrin, once it is formed, and in the general structure of the thrombus which seals a blood vessel It is also agreed that a diminution of platelets is frequently associated with an increase in capillary fragility and an increased tendency to bleed from small wounds Thus, there appears to be a positive correlation between platelets and vascular function For this reason the hemorrhagic diseases in which platelets are reduced may be included in those in which vascular defense has failed

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The findings at autopsy are chiefly those of extensive hemorrhage throughout the body The bone marrow in the usual patient shows the megakaryocytes present in normal or increased numbers Recent studies have indicated that there may also be qualitative changes in the morphology of the megakaryocytes such as the absence of platelet formation The bone marrow may

should therefore be taken with regard to drug intake

2 *Physical Agents* — Thrombocytopenic purpura in this category is most commonly the result of irradiation by roentgen rays radium or the products of nuclear fission

3 *Infections* — A variety of infections associated with septicemia have been reported to be complicated by thrombocytopenia Scarlet fever diphtheria and meningococcemia are among the more common

4 *Food Sensitivity* — Thrombocytopenic purpura has been reported as being the result of sensitivity to various foods including milk citrus fruits wheat and potatoes

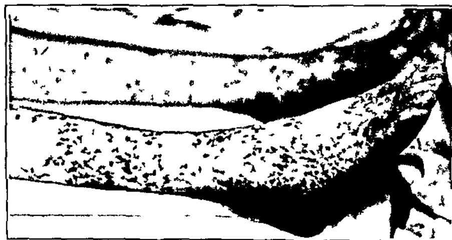


FIG 189 — Purpuric lesion in a case of scarlet fever There was no thrombocytopenia (Fox and Enzer Am Jour Med Sci)

There are some investigators who feel that most if not all cases of thrombocytopenic purpura may fall into this category Recent studies indicating the prevalence of eosinophils in the bone marrow in thrombocytopenic purpura may substantiate this theory However it is felt by most investigators that only a few cases are caused by food sensitivity

## SECONDARY (SYMPTOMATIC) THROMBOCYTOPENIC PURPURA

As indicated above thrombocytopenic purpura is often secondary to a generalized disorder of the bone marrow in which the megakaryocytes are actually mechanically displaced by other tissue This tissue may be leukemic tuberculous lymphomatous, carcinomatous, or fibrous or fatty in nature It may be erythroid tissue, as in pernicious anemia or in chronic hypochromic anemia

Thrombocytopenia may also be the result of disorders associated with enlargement of the spleen This type of thrombocytopenia is now thought to be part of the syndrome of hypersplenism in which the splenic tissue either destroys the platelets or secretes a hormone which affects maturation of the megakaryocytes or delivery of the platelets from the bone marrow Any of the splenomegalies may be associated with thrombocytopenia Among the more common ones are congestive splenomegaly Gaucher s disease Hodgkin s disease Felty s syndrome tuberculosis and sarcoid

## NONTHROMBOCYTOPENIC PURPURA

This type of purpura is characterized by a clinical syndrome milder than the thrombocytopenic variety and associated with normal platelets normal clot retraction and clotting time slight if any disturbance of bleeding time and a positive tourniquet test It may be associated with infections (Fig 189) or with drug ingestion and in some instances is associated with nutritional deficiency From the standpoint of strict

evident that there is incomplete consumption of prothrombin during the course of coagulation This seems to be due to a decrease in the amount of thromboplastin available for the conversion of prothrombin

Of considerable importance in the laboratory study of these patients is the bone marrow aspiration primarily for the purpose of excluding such conditions as leukemia pernicious anemia aplastic anemia, and lipoid reticuloendotheliosis In all these conditions, there will be diagnostic findings on bone marrow aspiration, whereas in the marrow of patients with idiopathic purpura there is little deviation from normal with the exception of a possible increase as well as morphologic changes in the megakaryocytes

Other changes in the blood are those which are the result of an acute and chronic blood loss

*Differential Diagnosis* —The differential diagnosis is primarily from other forms of thrombocytopenic purpura All the other hemorrhagic diseases are rather easily distinguished when the various laboratory tests for hemorrhagic diatheses are performed The differentiation from other forms of thrombocytopenic purpura will best be accomplished by a thorough history and physical examination bone marrow aspiration and biopsy of lymph nodes if these should be enlarged

*Treatment* —The treatment of this disorder falls into two general categories (1) expectant or conservative treatment with or without transfusions (2) splenectomy As indicated above approximately a third of the patients will have a spontaneous remission Splenectomy on the other hand will produce a remission in probably two-thirds of the cases In some of these cases splenectomy will be followed by a temporary rise in the number of platelets with a subsequent decrease in their number to below normal limits However even in this latter group there may be significant clinical improvement In other splenectomized patients there may be permanent improvement in all phases of the disease The chief reasons for delaying splenectomy in some patients are the occurrence of spontaneous remission, the fact that splenectomy is associated with a certain percentage of failures and the mortality rate connected with the operative procedure (about 5 per cent) Therefore, it would seem advisable to withhold splenectomy for two or three months in the hope of achieving a spontaneous remission In all patients when transfusions are indicated it is advisable to use blood less than 24 hours old It is felt also that the use of fresh blood definitely improves the result of splenectomy, particularly in the acute fulminating cases

A variety of other treatments have been suggested from time to time but none of these are sufficiently well documented to place them on the same basis as splenectomy or fresh blood transfusions Among these treatments are x irradiation of the spleen injection of moccasin venom, parathyroid hormone injections and ultraviolet irradiation of the body All patients should, of course receive a high protein high vitamin diet with ascorbic acid for general supportive treatment Recent preliminary studies by Bethell at Michigan and Lozner at Syracuse and Robson in Scotland indicate that adrenocorticotropic hormone and cortisone may be useful in this disorder These hormones have produced complete remissions in several patients which were sustained in some and transient in others In most patients the capillary fragility was favorably influenced during the period of administration of the hormones The exact role that these hormones will play in the treatment of this disorder is not clear, but they may be quite helpful in such situations as intractable epistaxis or menorrhagia

## TOXIC OR ALLERGIC THROMBOCYTOPENIC PURPURA

This type of purpura presents the same clinical picture as the idiopathic variety except that it is the result of known etiologic factors These factors may be enumerated as follows

1 *Drugs* —Many drugs are known to produce thrombocytopenic purpura Among these are the heavy metals—arsenic bismuth and gold Sulfonamides barbiturates and salicylates have all been reported as causing this disease A careful history

should therefore be taken with regard to drug intake

2 *Physical Agents* — Thrombocytopenic purpura in this category is most commonly the result of irradiation by roentgen rays radium or the products of nuclear fission

3 *Infections* — A variety of infections associated with septicemia have been reported to be complicated by thrombocytopenia Scarlet fever diphtheria and meningococcemia are among the more common

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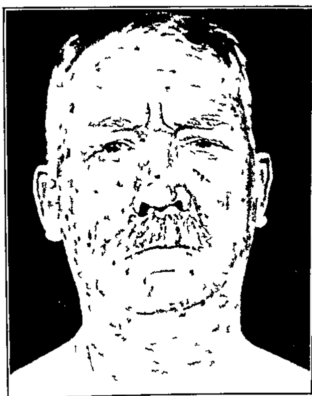
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definition, scurvy is such a nutritional deficiency. In addition to these etiological factors, there are the factor of allergy which is probably the most common one present in nonthrombocytopenic purpura, and the factor of unknown etiology, which has been termed thrombasthenia or pseudohemophilia. The latter term is mentioned only to be condemned for it has been applied to a variety of hemorrhagic diatheses of which nonthrombocytopenic purpura is but one. The term therefore has no definite meaning.

The allergic purpuras bear the names of Schoenlein and Henoch, the former having described a syndrome of purpura associated with arthralgia and an urticaria like eruption and the latter having described a syndrome of purpura and abdominal colic. There is considerable interchange however, between these two clinical syndromes and many patients have both joint involvement and colic. The manifestations may be the result of actual hemorrhage into the joint surface or into the intestinal muscosa. It is difficult, in most cases, to establish the antigen responsible for the purpura. However, many are benefited by elimination diets and by the use of either epinephrine or antihistaminic agents. The prognosis is, in general quite good.



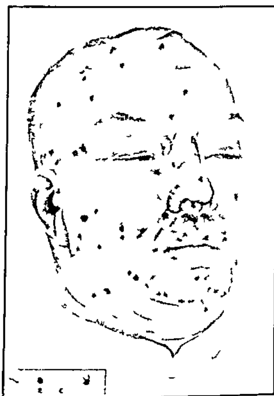


FIG 190 —Photograph and drawing of a patient aged fifty seven years who had suffered with hemorrhages from telangiectases since the age of twenty four. He later developed cirrhosis of the liver. The telangiectasia was familial. Four types of vascular lesions were present. *B* is the typical telangiectasi *D* is a spider angioma. (Wintrobe s Clinical Hematology )

## HEREDITARY HEMORRHAGIC TELANGIECTASIS

This is a hereditary vascular anomaly transmitted as a simple dominant trait involving both sexes and characterized by hemorrhage from the capillaries and venules of the skin and mucous membranes. The disease also bears the names of Osler Rendu and Weber who published early descriptions of it.

The characteristic sign is the presence of

multiple dilatations (telangiectases) of the capillaries and venules on the skin and mucous membranes and in all portions of the body (Figure 190) The family history is almost always positive The symptomatology is that of bleeding from the mucous membranes particularly from the nose There may be an associated anemia as the result of acute or chronic blood loss The treatment usually confines itself to cauterization when the bleeding point is accessible Transfusions may be necessary for acute bleeding and iron may be necessary for anemia of chronic blood loss Death from hemorrhage is rather unusual and life expectancy is in general within normal limits

## DISORDERS OF BLOOD COAGULATION

*Hemophilia —Definition —* This condition is an hereditary abnormality of the blood or blood forming systems It is exhibited only by males but is transmitted through females as sex linked Mendelian factor It is characterized by a chronic liability to hemorrhage which is dependent upon delayed coagulation of the blood

*Etiology —*The cause of the delayed coagulation time in hemophilia is still a source of much controversy One school of thought feels that there is a decrease in a globulin fraction of the plasma which is closely allied to thromboplastin This factor has been called "globulin substance plasma thromboplastin " and anti hemophilic globulin This theory is substantiated by the observation that platelet free plasma both *in vivo* and *in vitro* causes the clotting time of hemophiliacs to return toward normal Another theory is that the disorder is due to the presence of an anticoagulant in the plasma which is quite active against thromboplastin Still a third theory concerns the abnormal stability of the platelets and the failure to release thromboplastin in the course of blood coagulation Almost all recent studies have indicated that hemophilic platelets are quite comparable to normal platelets hence this third theory is at present in moderate disregard

*Incidence —* The disease is relatively uncommon It is transmitted from the male through an unaffected daughter, who is a carrier to a grandson The carrier daughters may also transmit the carrying potentiality to their daughters As a result of recent studies by Brinkhous of a form of hemophilia which occurs in dogs, it has been shown that if a hemophilic male dog mates with a female carrier, a hemophilic female results The absence of truly authenticated hemophilia in the human female is probably the result of the unlikelihood of the marriage of a hemophilic male to a female carrier About a third of all patients fail to give an adequate familial history of hemophilia This may be the result of transmission through several generations of daughters and incomplete knowledge by the patient of the family history or it may be due to an actual mutation

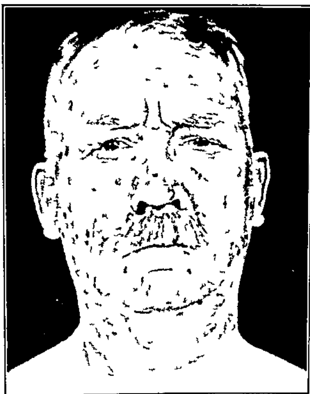
*Symptoms —*The characteristic symptom in hemophilia is the tendency to bleed from minor injuries and spontaneously into joints The excessive bleeding may appear within the first week of life as the result of circumcision Any mild trauma either accidental or intentional, such as a tooth extraction may cause prolonged or even fatal hemorrhage One of the most common and serious complications is hemorrhage into the joints which may result in a permanent deformity Hemorrhage into the joints first of all produces the findings of an acute hemarthrosis with severe pain and swelling and later the symptoms of chronic hemophilic arthritis with flexion deformities and arthralgias The knee joints are most frequently involved and next to these the elbow joints Almost every hemophiliac eventually develops the symptoms of chronic hemophilic arthritis with flexion deformities and muscle atrophy Epistaxis and hematuria are fairly common

*Signs —*Physical examination of the adult hemophiliac usually shows the signs of chronic hemophilic arthritis and there may be evidence of ecchymoses and hematomata and anemia

*Course —*The disease is rather unremitting in its course particularly as far as the hemarthroses and the development of hemophilic arthritis are concerned Adult life expectancy may be only slightly below normal if adequate treatment is given The state-

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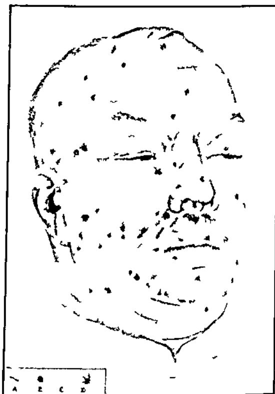



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*Signs.*—Physical examination of the adult hemophiliac usually shows the signs of chronic hemophilic arthritis and there may be evidence of ecchymoses and hematomata and anemia.

*Course.*—The disease is rather unremitting in its course, particularly as far as the hemarthroses and the development of hemophilic arthritis are concerned. Adult life expectancy may be only slightly below normal if adequate treatment is given. The state-

ment is usually made however, that the *majority of patients do not survive much* beyond childhood

*Diagnosis* —The diagnosis of this disease depends again upon the laboratory findings However the clinical syndrome of hemarthrosis leading to flexion deformities in a male is sufficiently characteristic to permit a clinical diagnosis in many instances

*Complications* —The complications are primarily those of the hemophilic arthritis and hemorrhages due to accidental or intentional trauma It is usually trauma which is responsible for death in most patients with hemophilia

*Laboratory Findings* —The characteristic laboratory finding is that of a delayed venous coagulation time By the Lee and White method, the normal clotting time will be between 4 and 12 minutes The clotting time of a hemophiliac will be from 20 minutes to several hours The results of all the other studies performed in the hemorrhagic diatheses such as bleeding time tourniquet test platelet count and prothrombin times are normal The blood findings are normal except for those which may be the result of acute or chronic hemorrhage The bone marrow examination is normal Tests based upon the ability of normal plasma to correct the deficiency in hemophilia have been devised However these not are usually necessary to establish the diagnosis

*Differential Diagnosis* —The differential diagnosis in hemophilia is primarily from other clinical hemorrhagic diatheses of moderate severity The normal blood findings, except for the greatly prolonged clotting time serve to eliminate most other hemorrhagic diatheses Of the diseases associated with a prolonged clotting time the chief disorders of interest are those of congenital afibrinogenemia and the recently described disorder associated with an anticoagulant

*Treatment* —The only treatment of any avail in hemophilia is the transfusion of relatively fresh blood or plasma or of the globulin fraction of plasma, which has been shown to have antihemophilic properties Use of the latter is still in the experimental stage and is not available for widespread use Relatively small volumes of blood or plasma suffice to shorten the clotting time toward normal, but it returns to its previous delayed time in from 12 to 48 hours In most hemophilic emergencies small transfusions given every 12 hours are usually quite effective in controlling the hemorrhage Larger transfusions are indicated as anemia supervenes The prevention of hemophilic emergencies by repeated transfusion of plasma has recently been attempted Other forms of treatment are the use of topical thrombin for the control of hemorrhage from mild trauma such as tooth extraction

## HYPOPROTHROMBINEMIA

The discovery of vitamin K by Dam in 1934 and of the prothrombin test and the prothrombin defect in jaundice by Quick and his colleagues in 1935 opened an entirely new era in the field of blood coagulation and hemorrhagic diathesis It is now clearly evident that vitamin K is necessary for the production of prothrombin by the liver Vitamin K is a fat soluble material and is found in food it is also synthesized by the bacteria of the intestines Vitamin K requires bile for its absorption Therefore if bile is excluded from the intestinal tract by such mechanisms as biliary obstruction or fistula, inadequate synthesis of prothrombin by the liver will ensue Hypoprothrombinemia may also occur as the result of failure of the newborn to be endowed with adequate amounts of vitamin K and prothrombin by the mother In all instances of hypoprothrombinemia except that associated with liver disease the administration of vitamin K restores the prothrombin concentration of the blood to normal

*Clinical Signs and Symptoms* —The hemorrhagic diathesis of hypoprothrombinemia is for the most part a mild one Ecchymosis and mucous membrane bleeding may be present as well as bleeding into the joints The most serious result of hypoprothrombinemia however is the one which follows major surgery in the absence of previous knowledge of the diminished prothrombin *concentration of the blood* It was this mechanism which accounted for the death of *many patients with jaundice* operated upon before the discovery of vitamin K

*Laboratory Findings and Diagnosis*—The diagnosis of hypoprothrombinemia cannot be made without the actual measurement of the prothrombin concentration of the plasma. Several methods for this determination have been devised. Probably the one devised by Quick or one of its modifications is most frequently used.

*Prevention of Hypoprothrombinemia*—As a result of the knowledge of clinical situations in which hypoprothrombinemia is apt to develop such as obstructive jaundice it is usually possible to prevent hypoprothrombinemia by early administration of vitamin K. In the case of the newborn, the vitamin K may be given to the mother during the last week of pregnancy by the use of the synthetic analogues of vitamin K in a dosage of 1-2 mgms daily by mouth. These may also be given to the newborn parenterally in a dosage of 1-2 mgms. Synthetic vitamin K may also be given in the case of pre-operative preparation of surgical patients. The dosage here need not exceed 2 mgms a day either.

*Treatment*—Once hypoprothrombinemia is discovered by the use of the prothrombin test treatment is indicated and this is best accomplished by the use of vitamin-K synthetic analogues which are water soluble. These can be given orally. The synthetic analogues of vitamin K are of very low toxicity and may be given in relatively large amounts. However in patients with normal liver function a dose not exceeding 10 mgms will usually suffice to bring the prothrombin to normal limits.

## HYPOPROTHROMBINEMIA AND LIVER DISEASE

Both in acute and in chronic liver disease it is often observed that the prothrombin time is prolonged. In this situation vitamin K is usually ineffective. It is this point which makes the use of vitamin K helpful in the differential diagnosis of jaundice. Where the jaundice is due to biliary obstruction and liver disease has not had an opportunity to develop the low prothrombin concentration will probably increase upon the administration of vitamin K. On the other hand where jaundice is due to hepatocellular disease the administration of vitamin K will be ineffective. The only therapy for the hypoprothrombinemia of liver disease is the transfusion of fresh blood or plasma.

*Hypoprothrombinemia and Dicumarol*—The discovery of dicumarol by Link and the hypoprothrombinemia produced by this agent represents a significant advance in the treatment of thromboembolic disease. Dicumarol because of its chemical resemblance to vitamin K competes with it in the liver synthesis of prothrombin and results in hypoprothrombinemia. This hypoprothrombinemia is useful in the treatment of coronary thrombosis or other thromboembolic diseases.

It is important to bear in mind that the administration of dicumarol must be followed up by the taking of daily prothrombin times for the effects of the drug may not manifest themselves for from 48 to 72 hours. During this time the drug may accumulate and cause serious hemorrhage unless it is administered with circumspection. The effectiveness of vitamin K preparations in the treatment of hypoprothrombinemia due to dicumarol toxicity is still somewhat in controversy. In general the best treatment aside from the obvious one of discontinuing the drug is the administration of fresh blood or plasma. Here too it is important to note that prothrombin concentration of the blood will rise rather slowly after the discontinuance of dicumarol and that there may be a latent period of 2 or 3 days before it begins to rise at all.

TABLE 62—CLASSIFICATION OF HEMORRHAGIC DISEASES ACCORDING TO PATHOLOGIC PHYSIOLOGY

- Failure of Vascular Defense (bleeding time usually increased and tourniquet test usually positive)
  - Thrombocytopenic Purpura (platelets decreased, clot retraction poor)
    - Idiopathic (Werlhof's disease: diminished formation of platelets from megakaryocytes in marrow; megakaryocytes usually normal or increased; eosinophils may be increased in marrow and blood)
    - Toxic or Allergic (history of drug ingestion, infection or hypersensitivity)
    - Secondary (symptomatic)
      - Disease of Bone Marrow (megakaryocytes mechanically displaced)
        - Leukemia
        - Pernicious anemia

Aplastic anemia
Chronic hypochromic anemia
Tuberculosis
Carcinomatosis
Lymphomatosis etc
Disease of Spleen (hypersplenism spleen almost invariably enlarged megakaryocytes in marrow present in normal numbers)
Congestive splenomegaly
Gaucher s disease
Felty s syndrome
Lymphomatosis
Tuberculosis
Sarcoid etc
Non thrombocytopenic Purpura (platelets normal clot retraction good)
Allergic
Henoch s purpura (*gastro-intestinal colic*)
Schonlein s purpura (rheumatic symptoms)
Toxic (drugs, uremia)
Infections (septicemias)
Nutritional (scurvy)
Thrombasthenia (usually hereditary)
von Willebrand s disease
Glanzmann s disease
Hereditary Hemorrhagic Telangiectasia
Osler Rendu Weber disease
Failure of Blood Coagulability Defense (venous clotting time usually increased)
Hemophilia (probably thromboplastin deficiency Prothrombin time normal exclusively in males sex linked Mendelian recessive hemarthroses common)
Hypoprothrombinemia (prothrombin time prolonged venous clotting time frequently normal)
Failure of Vitamin K Absorption (responds to vitamin K)
Due to exclusion of bile from intestine
Biliary obstruction
Biliary fistula
Due to Intestinal disease
Sprue
Colitis
Ileitis etc
Failure of Synthesis of Vitamin K by Intestinal Flora (responds to vitamin K)
Hemorrhagic disease of newborn
*Failure of Production of Prothrombin by Liver* (does not respond to vitamin K)
Cirrhosis
Hepatitis
Acute yellow atrophy
Fibrinogenopenia (absence of fibrinogen must be demonstrated by analysis)
Congenital
Acquired (liver disease)
Factor V Deficiency (disease described by *Owren*)
Circulating Anticoagulant (patient s plasma is anticoagulant for normal blood)
Heparin or Heparin like Substance (anaphylactic shock ? of irradiation)
Unknown (Disease described by Lozner Jolliffe and Taylor)

## BIBLIOGRAPHY


AGGELER P M and LUCIA S P Hemorrhagic Disorders A Guide to Diagnosis and Treatment The University of Chicago Press Chicago Ill 1949

MACFARLANE R G Critical Review The Mechanism of Hemostasis Quart J Med N S 1941 *10* 1

TOCANTINS I M Mechanism of Hemostasis. Ann Surg 1947 *125* 292

FROMMEYER W B and EPSTEIN R D Medical Progress Hemorrhagic Diseases New Eng J Med 1949 *241* 700 743

QUICK A J *The Hemorrhagic Diseases and the* Physiology of Hemostasis Charles C Thomas Springfield Ill 1942

DOAN C A The Etiology and Management of the Hemorrhagic Diatheses Ann Int Med, 1949 *31* 967

WINTROBE M M Clinical Hematology Lea & Febiger Philadelphia 1951

STURGIS C C Hematology Charles C Thomas Springfield Ill 1948

OWREN P A Coagulation of Blood Investigation on a New Clotting Factor Acta Med Scand Supplement, 1947 *194* 1

DEVRIES A ALEXANDER B and GOLDSTEIN R A Factor in Serum which Accelerates the Conversion of Prothrombin to Thrombin I Its Determination and Some Physiologic and Biochemical Properties Blood 1949 *3* 247

EPSTEIN R D, LOZNER E L COBBEY T S JR. and DAVIDSON C S Congenital Thrombocytopenic Purpura Purpura Hemorrhagica in Pregnancy and in the Newborn Am J Med 1950 *9* 44

DAMESHEK W and MILLER E B The Megakaryocytes in Idiopathic Thrombocytopenic Purpura A Form of Hypersplenism Blood 1946 *1* 27

QUICK A J SHANBERGE J N and STEFANINI M Coagulation Defect in Thrombocytopenic Purpura J Lab & Clin Med 1949 *34* 761

SCHWARTZ S O and KAPLAN S R Thrombocytopenic Purpura The Prognostic and Therapeutic Value of the Eosinophile Index An Analysis of 100 Cases Am J Med Sci 1950 *219* 528

DAMESHEK W and ESTREN S Hypersplenism Med Clin N Amer 1950 *34* 1271

LOZNER E L JOLLIFFE L S and TAYLOR F H L Hemorrhagic Diathesis with Prolonged Coagulation Time Associated with a Circulating Anticoagulant Am J Med Sci 1940 *199* 318

ALEXANDER B and LANDWEHR G Studies of Hemophilia I The Control of Hemophilia by Repeated Infusions of Normal Human Plasma J A M A 1948 *138* 174

DAVIDSON C S EPSTEIN R D MILLER G F and TAYLOR F H L Hemophilia A Clinical Study of Forty Patients Blood 1949 4 97

BRINKHOUS K M Plasma Prothrombin Vitamin K Medicine 1940 *19* 329

## CHRONIC CONGESTIVE SPLENOMEGALY (BANTI'S DISEASE)

By Cyrus C Sturgis, M D

*Synonyms* —Splenic anemia Fibrocongestive splenomegaly

*Definition* —This condition is a syndrome probably resulting from a circulatory disturbance of the spleen which is characterized by chronicity, a tendency to bleeding from the gastro intestinal tract splenomegaly, leukopenia frequently thrombocytopenia evidences of an increased collateral circulation between the portal and peripheral venous circulation and by certain constant anatomic changes in the spleen

*Etiology* —The cause of the syndrome is obscure Banti's original theory that it resulted from the action of some unknown toxic agent first on the spleen and later on the liver is no longer accepted It is probable that several causes may lead to one common result which is responsible for the condition William P Thompson believes that it is due to the mechanical obstruction of the blood from within the portal system which produces secondary congestive splenomegaly The obstruction may result from hepatic cirrhosis or to a variety of extrahepatic causes as thrombosis of the portal and splenic veins, compression of the veins by tumors or scars stenosis of the portal vein and possibly other developmental defects Ravenna suggests that the splenic congestion may be caused by lesion of the splenic arterioles which produce a circulatory disturbance in the portal bed

Regardless of the cause, the changes in the spleen are the same namely follicular atrophy fibrosis of the pulp with dilated venous sinuses the characteristic perifollicular hemorrhage and siderotic nodules

*Symptoms and Signs* —The condition usually appears before the age of thirty five years but may develop in childhood It is somewhat more common in females There is no hereditary tendency

The onset is usually gradual with the symptoms of anemia chiefly weakness ease of fatigue and pallor Commonly vague digestive complaints as abdominal discomfort and distention appear There may be diarrhea Enlargement in the upper left quadrant of the abdomen may be the first indication to the patient of the disorder or a large hematemesis or passage of tarry stools may inaugurate the disease Gross gastro intestinal bleeding occurs in about 50 per cent of the cases

Physical examination usually shows a moderate splenomegaly but in some instances the organ may be enormous filling the entire left side of the abdomen About one-third of the cases have moderate enlargement of the liver

*Blood* —An anemia averaging about 3,500 000 red blood cells per c mm is commonly present, and usually it is normocytic in type If there have been repeated hemorrhages it will be of the microcytic hypochromic variety With extensive involvement of the liver and in the absence of bleeding it may be of the macrocytic type

A leukopenia of less than 5000 cells per c mm and characterized by a reduction of all types of cells is almost always present and represents therefore one of the most constant findings of the disease There is often a moderate reduction in the number of platelets and sometimes they may be below 100 000 per c mm Occasionally evidence of a thrombocytopenic purpura may be present

*Prognosis and Treatment* —In many patients there are long periods of good health without manifestations of the disease Massive bleeding, however is unpredictable as it may occur at any time without warning Death results from bleeding liver insufficiency' or intercurrent disease

Treatment of the anemia includes transfusions following excessive hemorrhage iron if a microcytic hypochromic anemia is present and intramuscular injections of liver extract in a few patients who have a macrocytic anemia The diet should be high in protein and may be supplemented by yeast

The decision concerning splenectomy is the one which is difficult to make as the value of this procedure is not uniformly acknowledged A comparison of the course of the disease in patients in whom the operation has been performed has been said to

Aplastic anemia
Chronic hypochromic anemia
Tuberculosis
Carcinomatosis
Lymphomatosis etc
Disease of Spleen (hypersplenism spleen almost invariably enlarged megakaryocytes in marrow present in normal numbers)
Congestive splenomegaly
Gaucher s disease
Felty s syndrome
Lymphomatosis
Tuberculosis
Sarcoid etc
Non thrombocytopenic Purpura (platelets normal *clot retraction good)*
Allergic
Henoch s purpura (gastro intestinal colic)
Schonlein s purpura (rheumatic symptoms)
Toxic (drugs uremia)
Infections (septicemias)
Nutritional (scurvy)
Thrombasthenia (usually hereditary)
von Willebrand s disease
Glanzmann s disease
Hereditary Hemorrhagic Telangiectasia
Osler Rendu Weber disease
Failure of Blood Coagulability Defense (venous clotting time usually increased)
Hemophilia (probably thromboplastin deficiency Prothrombin time normal exclusively in males sex linked Mendelian recessive hemarthroses *common)*
Hypoprothrombinemia (prothrombin time prolonged venous clotting time frequently normal)
Failure of Vitamin K Absorption (responds to vitamin K)
Due to exclusion of bile from intestine
Biliary obstruction
Biliary fistula
Due to Intestinal disease
Sprue
Colitis
Ileitis etc
Failure of Synthesis of Vitamin K by Intestinal Flora (responds to vitamin K)
Hemorrhagic disease of newborn
Failure of Production of Prothrombin by Liver (does not respond to vitamin K)
Cirrhosis
Hepatitis
Acute yellow atrophy
Fibrinogenopenia (absence of fibrinogen must be demonstrated by analysis)
Congenital
*Acquired* (liver disease)
Factor V Deficiency (disease described by Owren)
Circulating Anticoagulant (patient s plasma is anti coagulant for normal *blood)*
Heparin or Heparin like Substance (anaphylactic shock ? of irradiation)
Unknown (Disease described by Lozner Jolliffe and Taylor)

## BIBLIOGRAPHY


Aggeler P M, and Lucia, S P *Hemorrhagic* Disorders A Guide to Diagnosis and Treatment. The University of Chicago Press Chicago Ill 1949
Macfarlane R G Critical Review The Mechanism of Hemostasis Quart J Med N S 1941 *10* 1
Tocantins L M Mechanism of Hemostasis Ann Surg 1947 *125* 292
Frommeyer W B and Epstein R D Medical Progress Hemorrhagic Diseases New Eng J Med 1949 *241* 700 743
Quick A J The Hemorrhagic Diseases and the Physiology of Hemostasis Charles C Thomas *Springfield Ill 1942*
Doan C A The Etiology and Management of the Hemorrhagic Diatheses Ann Int Med 1949 *31* 967
Wintrobe M M Clinical Hematology Lea & Febiger Philadelphia 1951
Sturgis C C Hematology Charles C Thomas Springfield Ill 1948
Owren P A Coagulation of Blood Investigation on a New Clotting Factor Acta Med Scand Supplement 1947 *194* 1
deVries A Alexander B and Goldstein R A Factor in Serum which Accelerates the Con *version of Prothrombin to Thrombin I Its* Determination and Some Physiologic and Biochemical Properties Blood 1949 *3* 247
Epstein R D Lozner E L Cobbey, T S Jr and Davidson C S Congenital Thrombocytopenic Purpura Purpura Hemorrhagica in Pregnancy and in the Newborn Am J *Med 1950 9* 44
Dameshek W and Miller E B The Megakaryocytes in Idiopathic Thrombocytopenic Purpura A Form of Hypersplenism Blood 1946 *1* 27
Quick A J Shanberge J N and Stefanini M Coagulation Defect in Thrombocytopenic Purpura J Lab & Clin Med *1949 34 761*
Schwartz S O and Kaplan S R Thrombocytopenic Purpura The Prognostic and Therapeutic Value of the Eosinophile Index An Analysis of 100 Cases Am J Med Sci 1950 *219* 528
Dameshek W and Estren S Hypersplenism Med Clin N Amer 1950 *34* 1271
Lozner E L Jolliffe L S and Taylor F H L Hemorrhagic Diathesis with Prolonged Coagulation Time Associated with a Circulating Anticoagulant Am J Med Sci 1940 *199* 318
Alexander B and Landwehr G Studies of Hemophilia 1 *The Control of Hemophilia by* Repeated Infusions of Normal Human Plasma J A M A 1948 *138* 174
Davidson C S Epstein R D Miller G F and Taylor F H L Hemophilia A Clinical Study of Forty Patients Blood 1949 4 97
Brinkhous K M Plasma Prothrombin Vitamin K Medicine 1940 *19* 329

## CHRONIC CONGESTIVE SPLENOMEGALY (BANTI S DISEASE)

By Cyrus C Sturgis M D

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The onset is usually gradual with the symptoms of anemia chiefly weakness ease of fatigue and pallor Commonly vague digestive complaints as abdominal discomfort and distention appear There may be diarrhea *Enlargement in the upper left* quadrant of the abdomen may be the first indication to the patient of the disorder or a large hematemesis or passage of tarry stools, may inaugurate the disease Gross gastro intestinal bleeding occurs in about 50 per cent of the cases

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be no different than in those who have not been operated upon. Certainly if there is evidence of extensive liver damage, the operation can do little good. In the absence of evidence of severe hepatic injury an abdominal exploratory operation should be seriously considered, and splenectomy performed if the liver appears to be reasonably normal in appearance.

REFERENCES

ROUSSELOT, L. M.: Role of Congestion (Portal Hypertension) on So-Called Banti's Syndrome: Clinical and Pathologic Study of Thirty-one Cases with Late Results Following Splenectomy. Jour. Am. Med. Assn. 1936, *107*, 1799.

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## MALIGNANT LYMPHOMAS

By CYRUS C. STURGIS, M.D.

*Classification.* — The classification of the lymphomas is confused: the clinical characteristics of the subtypes are not clean cut, and a histologic basis for differentiation is unreliable because a lymphoma may change from one type to another, vary from one lymph node to another or vary in type within the same lymph node.

*Interrelation Between Hodgkin's Disease and Other Lymphatic Tumors.* —Custer and Bernard (1948) after studying the interrelationship between Hodgkin's disease and other malignant lymphomas concluded that the cellular structure of the tumors was extremely labile, transitions from one type to another occurring frequently. The predominating cell pattern at any one examination may indicate one of the three forms of Hodgkin's disease (paragranuloma, granuloma or sarcoma), follicular lymphoblastoma, lymphosarcoma, reticulum-cell sarcoma, lymphatic leukemia or monocytic leukemia. *They believe that these terms are useful only to designate the predominating histologic pattern of a lymphoma at any one time. A rigid classification of lymphatic tumors therefore is not warranted. The entire group in their opinion may be regarded as a single neoplastic entity having a number of variants.*

Terms employed to designate the cellular pattern of a lymphoma at any given time are as follows:

1. Hodgkin's granuloma, paragranuloma and sarcoma (defined under Hodgkin's disease).
2. Follicular lymphoma (a lymphatic tumor, localized or multicentric, in which there is differentiation into follicles).
3. Lymphosarcoma (a tumor consisting of relatively uniform round cells, which may be small, well differentiated lymphocytes or large immature lymphocytes).
4. Reticulum-cell sarcoma (a tumor made up of very large cells with big nuclei. This type has been called "stem-cell lymphoma," "clasmatocytic lymphoma," etc. to indicate the highly undifferentiated form of the cells observed in this disease).
5. Mycosis fungoides, a condition now generally regarded as a neoplasm accompanied by tumor-like changes in the skin and ultimate histologic evidence of involvement of the superficial and deep lymph nodes, the bone marrow and other tissues with Hodgkin's disease, lymphosarcoma or lymphatic leukemia. The form usually encountered develops after a premycotic lesion characterized by a desquamative dermatitis with pruritus which may in some cases precede by years the formation of cutaneous tumors; on the other hand, the tumors may be the initial evidence of a lymphoma. The tumors are raised purplish red areas of infiltration usually exceeding three cubic centimeters in diameter. Ulceration occurs late in the disease.

## HODGKIN'S DISEASE

*Synonyms.* — Pseudoleukemia. Lymphoblastoma. Malignant lymphoma. Malignant lymphogranuloma. Lymphadenoma.

*Definition.* —A fatal disease, sometimes of long duration, of undetermined cause but most likely neoplastic or infectious in nature, characterized by typical histologic changes in lymph glands, spleen and other organs, by a painless, progressive, radiosensitive enlargement of lymph glands and, in the advanced stages, by fever, anemia and emaciation.

*Etiology.*—It is well recognized that the disease is observed in all races and is about twice as frequent in males as in females. It may occur in infancy and in extreme old age but the greatest incidence is in the third decade. The cause has been attributed to various types of infection including tuberculosis and an unidentified virus but it is now considered to be neoplastic in origin by a majority of students of the disease. Others believe however that it is of totally unknown origin.

*Relation to Tuberculosis.*—Between 15 and 20 per cent of all patients with Hodgkin's disease also have tuberculosis, but the cause of this association is not known. Furthermore in 80 to 85 per cent of the patients with Hodgkin's disease there is an anergy to tuberculin as evidenced by a negative tuberculin reaction. The presence of a positive reaction with tuberculin in high dilution in an untreated patient is evidence of active tuberculosis. The frequent association of the two diseases is possibly on the basis that Hodgkin's disease predisposes to tuberculosis or that the constitutional type which is predisposed to Hodgkin's disease also is more susceptible to infection with the tubercle bacillus.

*Pathology.*—There is usually a widespread involvement of both the superficial and deep lymph glands including the cervical, axillary, inguinal, mediastinal and abdominal glands. In size they vary from that of a pea to an orange. They are round, smooth, hard or soft depending on the stage of the disease and loosely held together with connective tissue. The glands are never firmly adherent to each other unless there has been a secondary infection. The characteristic microscopic picture is one of lymphoid hyperplasia with active proliferation of the germinal centers and the endothelial and reticular cells. Multinuclear giant cells and eosinophils are frequently observed. As the process advances there is an increase in connective tissue until the cellular part of the tumor is reduced to small areas lying between bands of fibrous tissue. While the condition primarily involves the lymph glands almost any organ of the body containing lymphatic tissue may develop the characteristic changes. The process is noted commonly in the spleen and less frequently in the liver and kidneys. The bone marrow may be infiltrated with lymphoid cells which in large part replace the erythroblastic tissue and thus produce a myelophthisic anemia.

Jackson and Parker have divided Hodgkin's disease into three subgroups: (1) Hodgkin's granuloma, the familiar type (90 per cent of all cases), the duration of life being a few years with the usual clinical picture. (2) Hodgkin's paragranuloma (the disease usually becomes apparent in the neck glands and runs a benign course; the histologic picture in the glands does not resemble true tumor). (3) Hodgkin's sarcoma (a true neoplasm as it is invasive). Hodgkin's sarcoma occurs most commonly in the fifth and sixth decades, rarely before thirty years of age. The life expectancy is brief.

*Symptoms.*—The most frequent initial symptom is a painless unilateral enlargement of a cervical lymph gland although the primary glandular enlargement may be in the axilla or inguinal regions or in the abdomen. The involvement often spreads rapidly to the other side of the neck and other superficial lymph glands. The enlarged nodes are usually firm, freely movable, not adherent to the skin or other glands and nontender. Occasionally however the earliest evidence of the condition may be loss of weight and weakness, fever, pruritis or cough and dyspnea.

As the disease progresses certain constitutional symptoms inevitably appear. Such complaints as weakness, loss of weight, pallor, dyspnea and palpitation are due entirely or in part to the associated myelophthisic anemia. Fever is present during the course of the disease in all cases. A striking type of the disease shows febrile periods persisting for two or three weeks alternating with afebrile periods of a week or ten days duration (Pel-Ebstein type). The presence of this type of fever, an anemia and leukopenia is suggestive of the diagnosis of Hodgkin's disease in the absence of other obvious cause of such changes.

A large variety of symptoms may result from the pressure of the enlarged glands upon nerves, blood or lymph vessels or various organs. Enlarged glands in the

be no different than in those who have not been operated upon. Certainly if there is evidence of extensive liver damage, the operation can do little good. In the absence of evidence of severe hepatic injury, an abdominal exploratory operation should be seriously considered and splenectomy performed if the liver appears to be reasonably normal in appearance.

REFERENCES

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plasma-cell infiltration In late cases, there may be hypoplasia of erythropoiesis

*Blood* —The blood changes are not sufficiently constant or characteristic to be of great aid in diagnosis In about a third of our patients, when first seen there was no anemia In the rest, there was slight or moderate progressive anemia, most frequently of the hypochromic normocytic type but in about 20 per cent of the hypochromic microcytic variety The red blood cells usually appear quite normal unless the anemia is severe An acquired hemolytic anemia with some degree of macrocytosis, the latter probably being associated with the presence of reticulocytes in the circulating blood is occasionally observed The white blood-cell count is normal or within 10 per cent of normal in almost all patients In some however it may be increased to 25 000 per cubic millimeter or even higher and in others a leukopenia with a white blood cell count as low as 2000 per cubic millimeter may be present, even in the absence of roentgen ray therapy A leukopenia is usually associated with the more advanced phases of the disease and may portend an ominous outlook

The two most common alterations on examination of a stained blood film are (1) an increase in the neutrophil percentage with a greater number of nonsegmented forms (this occurs almost constantly) and (2) an eosinophilia of greater than 10 per cent (this has however rarely been known to reach 70 per cent or more) There are frequently a relative lymphopenia and a monocytosis The platelets tend to parallel the white blood cell count and hence may be increased or decreased The sedimentation rate is almost always elevated when the disease is active The bone marrow shows no characteristic findings and hence from a diagnostic standpoint, its chief value is in ruling out leukemia

*Prognosis* —It is generally considered that Hodgkin s disease terminates fatally 2 or 3 years after the clinical onset In my opinion early treatment with roentgen ray and nitrogen mustards will frequently prolong life to an average of between 4 and 5 years although not all observers agree Experience has shown that almost 20 per cent of the patients will survive for at least 5 years and 5 per cent for 10 years, I have even observed a patient who was alive 21 years after the diagnosis of Hodgkin s disease had been established All agree that there is a wide variation in the length of life after onset of the disease the reason for this is unknown but it probably depends on some obscure inherent tendency of the disease process Patients with involvement limited to the upper cervical regions who receive early treatment do the best Those with palpable spleen and a white blood-cell count below 6000 or above 10 000 per cubic millimeter and those with anemia have the most unfavorable outlook When the syndrome of a Pel Ebstein fever, leukopenia and anemia is present the chances for survival of more than a few months is not great

*Pregnancy and Hodgkin's Disease* —In many cases Hodgkin s disease has apparently not interfered with pregnancy or the delivery of a normal child Roentgen ray therapy should be withheld during pregnancy to avoid harming the child *in utero* probably the only safe form of therapy for Hodgkin s disease in cases of pregnancy is blood transfusions

*Treatment* —Radical excision of the glands has been advised in the past but there are few advocates of this form of therapy at present Localized symptomatic roentgen-ray treatment is the treatment of choice and it is undoubtedly of great service It alleviates symptoms increases the survival period diminishes the size of the glands and improves the patient's sense of well being Roentgen ray therapy should be given when there is fever, anemia gland enlargement causing pressure on nerves or vital organs or apparent progression of any lesion The idea previously held that after a certain amount of roentgen therapy the patient became refractory to it is not necessarily true In my opinion the refractoriness develops as a result of progression of the disease regardless of the amount of $x$ ray therapy employed There is no evidence that radium is superior Radioactive elements such as phosphorus are not indicated Blood transfusions are of great value and should be given frequently in an attempt to maintain the hemoglobin at a minimum

mediastinum may cause the clinical picture of a mediastinal tumor with dyspnea cyanosis distention of the veins of the neck and edema of the face The trachea may be compressed and deviated Occasionally a patient is observed in whom the outstanding features are splenomegaly a moderate anemia, and fever Usually, however splenomegaly is not present unless the disease is advanced Dysphagia is not uncommon and pressure on the recurrent laryngeal nerves may result in aphonia Jaundice may be present as the result of pressure on the common bile duct by enlarged lymph glands, or in association with direct invasion of the liver by the pathologic process When a discharging sinus develops from a gland, which is rarely it is usually due to a concomitant tuberculosis

Abdominal symptoms are common and are the initial ones of the disease in some patients Abdominal pain simulating gallbladder disease or peptic ulcer may be present Additional complaints are diarrhea or constipation distention and diffuse abdominal tenderness The basis for these may occasionally be either multiple small ulcers of the stomach and bowel or infiltration of the wall in the areas affected The mediastinum the lung parenchyma the hilar nodes, and the pleura with or without an accumulation of fluid may be affected the greatest incidence of involvement being in the order named The possibility of a complicating amyloidosis should be kept in mind if an excessive amount of protein appears in the urine or a generalized anasarca develops in a patient with Hodgkin s disease Osteolytic or less commonly osteoblastic granulomatous foci occur in from 5 to 15 per cent of the patients These are more frequently observed in the order named vertebral column pelvis ribs upper ends of the femurs and the sternum Pain in the back either with or without erosion of the spine is occasionally a prominent symptom and may arise from spinal nerve root involvement A spastic paraplegia has been known to occur from invasion or compression of the spinal cord Pain in the legs is a common symptom late in the disease but it may occur early In Hodgkin s granuloma the neurological involvement arises by extension from the cranial bones or vertebræ to the dura, or from the development of an epidural tumor without bone lesions There are no proved cases in which the substance of the brain has been involved primarily, although this may occur in patients with Hodgkin's sarcoma, reticulum-cell sarcoma or lymphatic leukemia Cutaneous manifestations occur in about one-third of the patients, although often they are of minor significance An extreme degree of pruritus may be an early and annoying symptom which sometimes constitutes the patient s chief complaint In some patients there may be a generalized brownish pigmentation, or the discoloration may be irregularly distributed giving a mottled appearance Occasionally there may be an actual infiltration of the skin producing small nodules, or a generalized exfoliative dermatitis, or purplish-red tumor like cutaneous masses These masses are like those characteristic of the syndrome of mycosis fungoides

*Diagnosis* —The presence of a painless enlarged lymph gland appearing without obvious cause, should at once suggest the possibility of Hodgkin s disease In all such cases a small gland should immediately be excised and examined microscopically by a competent pathologist The patient should be carefully examined for evidence of other glandular enlargement including roentgenograms of the chest to determine the presence or absence of enlargement of the mediastinal glands In some, the clinical picture may be that of chills and fever without obvious cause In such patients there is usually enlargement of the superficial lymph glands but this may not occur until late in the disease Others have splenomegaly and a hypochromic anemia without superficial glandular enlargement which suggests the possibility of Banti s disease

*Sternal Aspiration* —Marrow thus obtained does not show specific changes and is of chief value in ruling out leukemia although the findings have some confirmatory value in suspicious cases The marrow is usually cellular and the myeloid-erythroid ratio is normal The myeloid cells show a shift to the left, which is evidence of immaturity There is an eosinophilic and

Custer R P and Bernhard W G The Inter Relationship of Hodgkin s Disease and Other Lymphatic Tumors Am J Med Sci 1948 *216* 625

Gall E A and Mallory T B Malignant Lymphoma Am Jour Path 1942 *18* 381

Goldman L B Hodgkin s Disease Analysis of Two Hundred and Twelve Cases Jour Am Med Assn 1940 *114* 1611

Jackson H Jr and Parker F Jr Hodgkin s Disease and Allied Disorders Oxford University Press New York 1947

Kasdon S C Pregnancy and Hodgkin s Disease with a Report of Three Cases Am J Obst and Gynec 1949 *57* 282

Pearson O H Eliel L P Rawson R W Konrad D and Rhoades C P ACTH—and Cortisone—Induced Regressions of Lymphoid Tumors in Man Cancer 1949 *2* 943

Sparling H J Jr Adams R D and Parker F Jr Involvement of the Nervous System by Malignant Lymphoma Medicine 1947 *26* 285

Symmers D Lymphoid Diseases Hodgkin s Granuloma Giant Follicular Lymphadenopathy Lymphoid Leukemia Lymphosarcoma and Gastro-intestinal Pseudoleukemia Arch Pathology 1948 *45* 73

## AGRANULOCYTOSIS

By Cyrus C Sturgis M D

*Synonyms* —Agranulocytic angina Malignant neutropenia Acute granulopenia Granulocytopenia

*Definition* —Agranulocytosis is a disease almost always due to a drug sensitivity, characterized by secondary infection with chills fever and ulcerative lesions in the mouth throat rectum vagina and sometimes elsewhere in the body There is a remarkable reduction or complete disappearance of the polymorphonuclear cells in the peripheral blood and in untreated patients often a rapidly fatal course

*Etiology* —The disease most commonly affects adults between the ages of 25 and 65 years and females twice as commonly as males Children occasionally have the condition as do infants one having been reported with the disorder possibly due to sepsis on the third day of life

Roberts and Kracke have presented a logical theory concerning the mechanism of the production of the disease as follows (1) there is the onset in the bone marrow with a failure of myelocytic function which may be due to myelocytic aplasia or cessation of maturation (maturation arrest) (2) after a few days there is a gradual diminution of the granulocytes in the peripheral blood until they may disappear or number only a few hundred per c mm (3) there is the clinical onset with the appearance of the characteristic symptoms (4) with the loss of protection bacterial invasion begins (5) recovery, or death follows

It has been suggested that the initial failure of the bone marrow which is the fundamental basis for the disease is due to sepsis, allergy or some endocrine disturbance There is little evidence to support these theories and it has now been firmly established that the condition is almost always the result of a sensitivity to drugs The following have been established as unquestionably causing the disease in patients who have a sensitivity to them (1) the sulfonamide drugs including prontosil sulfanilamide sulfapyridine sulfathiazole sulfadiazine succinyl sulfathiazole sulfaguanidine and sulfamerazine (2) thiourea and derivatives as thiouracil propylthiouracil and methylthiouracil (3) aminopyrine and closely related drugs as novaldin and causalin (4) gold (5) dinitrophenol (6) organic arsenicals as arsphenamine neoarsphenamine and mapharsen (7) presidon (pyrithyldione) (8) antihistaminic drugs as pyribenzamine diatrin and possibly other closely allied preparations (9) mustard gas (10) urethane Of alleged etiologic relationship but probably rarely if ever the cause of the condition are the barbiturates antipyrine neostibosan quinine and quinidine bismuth nirvanol plasmoquin trinitrotoluene chloromycetin tridione and mesantoin The two latter employed in convulsive states may cause a moderate selective depression of the granulocytes in the peripheral blood and, in severe involvement an aplastic anemia They do not however cause the typical syndrome of agranulocytosis

It should be recognized that the drugs known to cause the disease do so only in an exceedingly small percentage of the patients to whom they are given It must be assumed therefore that these substances can produce

level of approximately 11.0 grams per 100 cc of blood (70 per cent) Arsenic in the form of Fowler's solution may be employed as in myelogenous leukemia, but the results are greatly inferior to irradiation

*The Nitrogen Mustards* —The introduction of these preparations has been a distinct advance in the treatment of Hodgkin's disease and allied disorders The most commonly used members of this group are methyl bis (betachloroethyl) amine hydrochloride, or HN 2, and S K 136 which is a double nitrogen mustard thought to have the same effect Although the latter produces toxic effects less frequently they are more severe and prolonged when they do occur, even toxic psychoses have been noted The dose of each preparation is 0.1 milligram per kilo of body weight the dose to be given intravenously by injecting it into the rubber tubing of a free flowing intravenous saline-infusion set to avoid irritation of the vein and the surrounding tissue Such an injection is given every other day for four doses but in no instance should the total of the four doses exceed 24 milligrams The mode of action is similar to that of the roentgen rays and at present is thought to be chiefly a reaction with some nuclear component of the cell The treatment has been employed with success in various types of lymphoid disorders especially in Hodgkin's disease lymphosarcoma, follicular lymphoblastoma mycosis fungoides, and reticulum cell sarcoma

The indications for use of the nitrogen mustards in Hodgkin's disease and allied disorders are (1) the presence of the generalized form in which some of the involved areas are inaccessible to irradiation (2) The futility of further roentgen therapy (3) a white blood-cell count of 3500 per cubic millimeter or higher (4) the presence or threat of post irradiation changes (5) involvement of the nervous system or obstructive mediastinal tumors (post irradiation swelling undesirable)

The favorable effects of the nitrogen mustards may appear within a few days There is prompt recession of the enlarged lymph nodes and the spleen the fever itching cough, chest pain, and central nervous-system symptoms often disappear and the general condition of the patient improves promptly Mediastinal enlargements pleural effusions and ascites are more resistant The effects are purely palliative as the duration of the improvement may be limited to as short a time as one month, although in other patients, the improvement may last for several months or a year or longer There is clear evidence that an additional therapeutic effect may be attained by nitrogen mustard after roentgen ray therapy is no longer effective Furthermore, it is thought by some that patients refractory to x ray may become resensitized to this agent by nitrogen mustard There is also some evidence to suggest that the roentgen rays may re ensitize a patient resistant to nitrogen mustard

*Toxic Effects and Contraindications to Nitrogen Mustards* —Nausea and vomiting follow treatment in almost every patient They may occur after some injections and not after others Rarely do they persist for longer than 8 hours except occasionally when S-K 136 is given Gastrointestinal bleeding has seldom occurred In a few instances, mild anemia and thrombocytopenia have developed The limiting factor to the treatment is the leukopenia which may become extreme within a few days falling to as low as 400 white blood cells per cubic millimeter It is not advisable to employ this form of treatment when the white blood cell count is below 3500 per cubic millimeter

Recently Pearson and his associates (1949) have administered ACTH and cortisone in four divided doses totaling from 100 to 200 milligrams daily to a group of patients with lymphoid tumors In six patients there was a dramatic and progressive decrease in the size of the enlarged lymph nodes and of the enlarged spleens but in none of the patients was a complete clinical remission obtained These studies have not however established the efficacy of ACTH and cortisone as therapeutic agents in these conditions and the likelihood that they will produce only temporary benefit is great

REFERENCES

Bayer R D and Lar L A The Clinical Effect of Nitrogen Mustard on Neoplastic Diseases Am J Med Sci 1950 219 16

Custer R P and Bernhard W G The Interrelationship of Hodgkin s Disease and Other Lymphatic Tumors Am J Med Sci 1948 *216* 625
Gall E A and Mallory T B Malignant Lymphoma Am Jour Path 1942 *18* 381
Goldman L B Hodgkin s Disease Analysis of Two Hundred and Twelve Cases Jour Am Med Assn 1940 *114* 1611
Jackson H Jr and Parker F Jr Hodgkin s Disease and Allied Disorders Oxford University Press New York 1947
Kasdon S C Pregnancy and Hodgkin s Disease with a Report of Three Cases Am J Obst and Gynec 1949 *57* 282
Pearson O H Eliel, L P Rawson R W Konrad D and Rhoades C P ACTH—and Cortisone—Induced Regressions of Lymphoid Tumors in Man Cancer 1949 *2* 943
Sparling H J Jr Adams R D and Parker F Jr Involvement of the Nervous System by Malignant Lymphoma Medicine 1947 *26* 285
Symmers D Lymphoid Diseases Hodgkin s Granuloma Giant Follicular Lymphadenopathy Lymphoid Leukemia Lymphosarcoma and Gastro-intestinal Pseudoleukemia Arch Pathology 1948 *45* 73

## AGRANULOCYTOSIS

By Cyrus C Sturgis M D

*Synonyms* —Agranulocytic angina Malignant neutropenia Acute granulopenia Granulocytopenia

*Definition* —Agranulocytosis is a disease almost always due to a drug sensitivity characterized by secondary infection with chills fever and ulcerative lesions in the mouth throat rectum vagina and sometimes elsewhere in the body There is a remarkable reduction or complete disappearance of the polymorphonuclear cells in the peripheral blood and in untreated patients often a rapidly fatal course

*Etiology* —The disease most commonly affects adults between the ages of 25 and 65 years and females twice as commonly as males Children occasionally have the condition as do infants one having been reported with the disorder possibly due to sepsis on the third day of life

Roberts and Kracke have presented a logical theory concerning the mechanism of the production of the disease as follows (1) there is the onset in the bone marrow with a failure of myelocytic function which may be due to myelocytic aplasia or cessation of maturation (maturation arrest) (2) after a few days there is a gradual diminution of the granulocytes in the peripheral blood until they may disappear or number only a few hundred per c mm (3) there is the clinical onset with the appearance of the characteristic symptoms (4) with the loss of protection bacterial invasion begins (5) recovery, or death follows

It has been suggested that the initial failure of the bone marrow which is the fundamental basis for the disease is due to sepsis allergy or some endocrine disturbance There is little evidence to support these theories and it has now been firmly established that the condition is almost always the result of a sensitivity to drugs The following have been established as unquestionably causing the disease in patients who have a sensitivity to them (1) the sulfonamide drugs including prontosil sulfanilamide sulfapyridine sulfathiazole sulfadiazine succinyl sulfathiazole sulfaguanidine and sulfamerazine (2) thiourea and derivatives as thiouracil propylthiouracil and methylthiouracil (3) aminopyrine and closely related drugs as novaldin and causalin (4) gold (5) dinitrophenol (6) organic arsenicals as arsphenamine neoarsphenamine and mapharsen (7) presidon (pyrithyldione) (8) antihistaminic drugs as pyribenzamine diatrin and possibly other closely allied preparations (9) mustard gas (10) urethane Of alleged etiologic relationship but probably rarely if ever the cause of the condition are the barbiturates antipyrine neostibosan quinine and quinidine bismuth nirvanol plasmoquin trinitrotoluene chloromycetin tridione and mesantoin The two latter employed in convulsive states may cause a moderate selective depression of the granulocytes in the peripheral blood and in severe involvement an aplastic anemia They do not however cause the typical syndrome of agranulocytosis

It should be recognized that the drugs known to cause the disease do so only in an exceedingly small percentage of the patients to whom they are given It must be assumed therefore that these substances can produce

the disease only in persons who are sensitive to them.

There is a remarkable form called *recurrent or cyclic agranulocytosis* in which the episodes have the identical clinical and hematological aspects of the acute attacks. Such a condition is rare. It occurs at all ages from infancy to old age and appears to predominate in females. It is characterized by recurrent attacks every two or three weeks of fever, chills, and ulcerative lesions in the mouth and throat, with a striking decrease in the total white blood cell count and a reduction or complete disappearance of the neutrophils from the circulating blood. These attacks may occur over a long period; the longest such period on record is 34 years. The attacks have been attributed to cyclic infections, to endocrine disturbances, to deficiency in some factor controlling the development of the neutrophils in the bone marrow, but none of these explanations has been substantiated. Apparently the attacks are not associated with sensitivity to any type of medication, and overactivity of the spleen is not the cause (though improvement may follow splenectomy).

A *chronic* type of *agranulocytosis* has been described in which the manifestations are vague, consisting mainly of chronic fatigue and weakness associated with only a moderate depression of the white-blood cell count and neutrophil percentage. Such a condition, however, is rare and the clinical picture is ill defined.

*Primary splenic neutropenia* is a condition in which the total white blood cell count and neutrophil percentage may be greatly reduced over a long term of years (Wiseman and Doan 1939). It should not be confused with agranulocytosis, for primary splenic neutropenia is probably due to hypersplenism, which results in some cases in a selective destructive action on the neutrophils of the circulating blood with a resultant granulocytopenia. In such cases there are (1) splenomegaly, (2) neutropenia, (3) unimpaired production of neutrophils in the bone marrow, and (4) demonstration of splenic overactivity by the epinephrine test. Splenectomy usually affords relief.

*Symptoms and Signs*.—The clinical picture of acute agranulocytosis is that of a combination of sepsis of varying intensity but often severe, with ulcerative lesions of the mucous membranes, *usually of the mouth* and throat but sometimes of the vagina and rectum or other areas. The onset may be abrupt, with *fever, chills, sore* throat, and extreme prostration. Delirium may appear early. The ulcerative lesions may also occur throughout the entire alimentary tract, from esophagus to anal canal. Such lesions are not infrequently in the vagina and on the vulva; in a few instances they have been found on the conjunctiva. Often the condition is a fulminating one, but occasionally there may be only slight soreness of the throat with a mild febrile reaction. Necrosis of the skin is a rare complication, as is jaundice. The latter is due to hepatitis and gives an unfavorable prognosis.

The liver and spleen are not enlarged, and there is no generalized adenopathy, but the lymph glands draining the ulcerative lesions in the mouth and throat are usually enlarged and tender. In about half the fatal cases, there is evidence of a bronchopneumonia. This is a common cause of death, especially among the older patients.

*Blood*.—The striking feature is a pronounced leukopenia which may progress to such an extent that the polymorphonuclear *neutrophil cells completely disappear from* the peripheral blood. The reduction at first is only in the granulocytes, but later the *lymphocytes and monocytes* are also diminished. The total leukocyte count may be reduced to a few hundred cells per cubic millimeter. There is no alteration in the red blood cells unless a preexisting anemia is present or the illness is long continued, and then a slight to moderately severe anemia with a low color index may develop. The platelets are usually normal or increased except when the illness is prolonged, and they may then become diminished.

*Sternal Aspiration*.—The bone marrow shows either *myeloblastic hyperplasia* with arrest of maturation at the promyelocytic myelocytic stage but with normal erythropoiesis and thrombopoiesis, or *aplasia of the granulocytic system* with little involvement of the precursors of the erythrocytes or platelets. In the latter condition the prognosis is poor.

*Diagnosis*—The diagnosis is based upon the occurrence of a brief illness with an acute onset in an adult who has ingested one of the known causative agents and develops sepsis and ulcerative lesions of the mucous surfaces With these symptoms there is a decrease in circulating granulocytes which exceeds any other condition observed in clinical medicine and an *absence* of splenomegaly hepatomegaly immature white corpuscles in the blood stream, and a severe anemia It is most frequently confused with the leukopenia of severe sepsis aplastic anemia and subleukemic leukemia

*Prognosis and Treatment*—Agranulocytosis must always be considered a serious disease in which the outlook is ominous unless adequate and early treatment is given In the earlier series of cases the mortality rate was approximately 75 per cent but with effective treatment it was reduced to 25 per cent At present with the energetic use of anti biotic preparations to combat infection the outlook is greatly improved If the patients are seen early and the proper therapeutic measures are instituted promptly, the condition is seldom fatal There is an equal mortality in the two sexes

The most serious outlook is for patients over sixty The best prognostic indication is the general condition of the patient The following manifestations however have a serious significance—delirium extreme prostration necrotic lesions of the skin pneu monia jaundice a leukocyte count below 1000 per c mm or a complete absence of polymorphonuclear cells from the blood stream

The two most important aspects of treat ment are (1) discovering and eliminating the drug causing the condition and (2) treating the complicating infection early and efficiently with antibiotic preparations The diagnosis established a culture should be obtained at once from the patient s mouth and blood stream the organism isolated and sensitivity tests with the various anti biotics performed Without waiting for the results of these studies energetic antibiotic treatment should be instituted Since the mouth organisms are usually staphylococci and streptococci 400 000 units of penicillin should be given intramuscularly every 4 hours (2 4 million units every 24 hours) In addition if the patient is elderly or in an obviously serious condition 0 5 gram of aureomycin in 500 cc of normal saline solution should be injected intravenously by the slow drip method every twelve hours The penicillin should be continued in the dosage indicated above till the patient s temperature has been normal for at least 4 or 5 days and his general condition has greatly improved After a few days the aureomycin may be given orally (2 0 to 4 0 grams a day in capsules) If these preparations do not benefit the patient the results of the sensitivity tests should serve as a guide to further therapy In some cases streptomycin chloromycetin terramycin or other preparations may be indicated

The patient s tendency to recover spontaneously after the causative drug has been eliminated has confused the claims for various forms of therapy In my opinion however there is no convincing evidence that pentnucleotide, folic acid pyridoxine yellow bone marrow concentrate liver extract or stimulating doses of roentgen ray are of value If the patient s course is downhill I would not hesitate to give 2 or 3 blood transfusions of 500 cc each they may be helpful and can do no harm I would not use sulfonamide drugs in some cases they may cause agranulocytosis Besides the antibiotic preparations are more effective and have fewer side effects

The local treatment of the infected mouth and throat should be only with mouth washes and gargles of warm normal saline solutions Radical measures are to be avoided The fluid intake should be maintained adequately by intravenous saline and 5 per cent glucose injections if necessary The diet should be liquid or soft

*Prevention of Agranulocytosis*—When a patient is receiving a drug known to cause agranulocytosis it is not feasible to do leukocyte counts at frequent intervals as a prophylactic measure Even if this were done it would not always give warning that the disease was impending for the condition manifests itself first in the bone marrow—the changes in the white blood-cell count occur later Furthermore a severe leukopenia may develop within a few hours

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in the marrow and in the blood in leukemic cases is the blast form with the single exception that in some of the acute leukemic lymphocytic leukemias it is a cell indistinguishable morphologically from the lymphocyte or prolymphocyte Except in the lymphocytic type cells more differentiated than the pro-stage of the involved series are rare or absent

*Subacute leukemias* are defined as leukemias in which the expected duration of life is from three months to one year from the onset of the first symptom The onset is more insidious than in acute cases but all cases develop fever stomatitis and bleeding into the skin from the gums and mucous membranes within three months from the onset of symptoms The predominant cell in the marrow and blood in leukemic cases is the pro-stage of the involved series and an increased number of blast cells is always found Except in the lymphocytic type cells more differentiated than the pro-stage of the involved series are rare or absent

*Chronic leukemias* are defined as leukemias in which the expected duration of life is from one to twenty years or more the average being from three to five years depending on the type from the onset of the first symptom Fever stomatitis and hemorrhages into the skin or from the gums and mucous membranes rarely develop within the first year The most differentiated stage of the involved series is always present in addition to the less differentiated cells In the lymphocytic type only the lymphocyte is usually found and prolymphocytes are rare or absent

Provision is made so that the leukemias can be further subdivided into leukemic subleukemic and aleukemic forms

*Leukemic leukemias* are defined as leukemias in which the leukocyte count in the blood is above 15 000 per cu mm and the type cells are present in the blood in sufficient number to permit the diagnosis of the type of leukemia

*Subleukemic leukemias* are defined as leukemias in which the leukocyte count in the blood is below 15 000 per cu mm It is often much below normal in the 100 to 4000 range yet the typical cells of the particular variety of leukemia are present in the blood in sufficient numbers to suggest the diagnosis

*Aleukemic leukemias* are defined as leukemias in which the leukocyte count in the blood is below 15 000 per cu mm often as low as 100 to 4000 per cu mm but the typical cells either are absent or are so few usually less than one per 1000 cells that it is impossible to make the diagnosis from examination of the blood alone

In all aleukemic and most subleukemic leukemias marrow examination is essential to establish the diagnosis

*Incidence* —Leukemia has been observed in many species of warm blooded animals and occurs in all races of mankind Generally speaking the disease is more common in males than in females but the ratio of males to females affected varies at different age periods and with the type of leukemia present Lymphocytic leukemia for example has a decidedly higher incidence in males at all age periods and this is especially true of the chronic form in older persons In one series of cases studied at the Simpson Memorial Institute 80 per cent of the females with chronic lymphocytic leukemia were less than 60 years old when first observed whereas 60 per cent of the men were over the age of 60 On the other hand chronic granulocytic leukemia the most common form of the disease in middle life occurs almost as frequently in females as in males Acute leukemia and subacute leukemia affect persons in all age groups but occur most frequently in children and young adults in whom chronic leukemia is uncommon Before puberty there is little difference in the sex incidence of acute leukemia

The incidence of leukemia in the general population is difficult to estimate The Metropolitan Life Insurance Company reports that leukemia takes more than 6000 lives annually in the United States many of them children The death rate reported from leukemia is said to have more than doubled in twenty five years and is more than five times that of infantile paralysis about one and a half times that of measles scarlet fever whooping cough and diabetes combined and almost equal to that of appendicitis

From a practical standpoint, it suffices to warn the patient that taking a drug known to cause the condition may cause infection with fever, chills and sore throat. If these symptoms develop the patient should discontinue the medication immediately and have a leukocyte count made. If a leukopenia is present, antibiotic therapy should be begun at once. Such precautions should prevent a death as a result of the disease.

REFERENCES


DAMESHEK, W.: Leukopenia and Agranulocytosis. Oxford University Press, New York, 1944.

PLUM, P.: Clinical and Experimental Investigations in Agranulocytosis with Special Reference to the Etiology. Copenhagen, NYT Nordisk Forlag Arnold Busck, 1937.

REIMANN, H. A., and DEBARADINIS, C. T.: Periodic (Cyclic) Neutropenia, an Entity; a Collection of 16 Cases. Blood, 1949, 4, 1109.

YOUNG, C. J.: Leukocytic Count in the Prevention of Drug Agranulocytosis. Brit. M. J., 1949, 2, 261.


## LEUKEMIA

By FRANK H. BETHELL, M.D.

*Definition.*—Leukemia is a fatal disease of unknown etiology characterized by excessive and disordered proliferation of leukocytes and their precursors and by varied systemic manifestations resulting from disturbed hemopoiesis and from tissue infiltration.

*Classification.*—Leukemia, according to the view held by most students of the disease, constitutes a malignant neoplasm of leukocyte forming tissue. Therefore it is appropriate to include the leukemias with the malignant lymphomas under the general heading of *Neoplasms of the Hemic and Lymphatic Systems.* Further classification is based upon the cell type involved in the disease, the degree of functional differentiation or maturation of the predominant cells in the circulating blood, bone marrow or lymph tissue, the clinical course and the numerical range of the circulating leukocytes.

As is true of hematologic nomenclature generally, a varied and confusing terminology has been applied to the leukemias. Thus to designate chronic leukemia involving the granulocyte cells of the bone marrow such terms as *myelogenous, myeloid, myelocytic, myelosis, myelemia, myelocythemia, granulocytic, neutrophilocytic* and *leukemic myeloblastoma* have been used synonomously. Multiplicity of terms without defined differences of meaning also characterizes the nomenclature of leukemia affecting the cells of the lymphocytic and monocytic tissues.

In order to provide a system of terminology which would have the merits of uniformity, consistency, comprehensiveness and clarity, the Committee for Clarification of the Nomenclature of Cells and Diseases of the Blood and Blood Forming Organs has recommended that leukemias be classified according to the appropriate cell series and further subdivided as acute, subacute, or chronic and as leukemic, subleukemic or aleukemic. The list of recommended terms follows.

LEUKEMIA

Type unclassified*
Lymphocytic**
  Acute
    Leukemic
    Subleukemic
    Aleukemic
  Subacute
    Leukemic
    Subleukemic
    Aleukemic
  Chronic
    Leukemic
    Subleukemic
    Aleukemic
Granulocytic
  Neutrophilic
  Eosinophilic
  Basophilic
Monocytic
Plasmocytic
Megakaryocytic

* Under this heading may be included such designations as undifferentiated blast cell, stem cell or hemocytoblastic leukemia.

** Each type of leukemia can be subdivided as is indicated for the lymphocytic type.

*Acute leukemias* are defined by the Nomenclature Committee as those in which the expected duration of life is three months or less from the onset of the first symptom. The onset is typically with fever, stomatitis and bleeding into the skin, from the gums and mucous membranes. The predominant cell

types of leukemia are conveniently considered under appropriate headings

1) *Pressure manifestations* due to enlarged lymph nodes spleen or liver and occasionally to myeloid tumors

2) *Tissue infiltration* especially of bone marrow skin digestive tract, kidneys lungs heart, central nervous system and skeletal system

3) *Circulatory disturbances* including anemia hemorrhage, thrombosis and infarction

4) '*Toxic and hypermetabolic manifestations* including fever sweating nervousness heat intolerance, and weight loss

5) *Diminished resistance to infection* especially involving skin mucous membranes and respiratory tract

## CHRONIC GRANULOCYTIC LEUKEMIA

### (Myelogenous Myeloid Myelocytic Leukemia)

The onset of chronic granulocytic leukemia is gradual and the diagnosis may be made in the course of examination for an unrelated illness although accidental recognition is more common of chronic lymphocytic leukemia Usually the disease is well advanced when the patient is first seen and the presenting complaints are most often referable either to anemia or enlargement of the spleen They include increasing fatigability weakness shortness of breath on exertion abdominal fullness and discomfort after eating and not infrequently pain occurring in the left upper quadrant sometimes referred to the left shoulder region and attributable to splenic infarction and diaphragmatic involvement Slight irregular fever is common when the disease is moderately well advanced and the temperature almost always rises to high levels in the terminal phase Symptoms due to increased metabolism may be prominent Purpura and a generalized hemorrhagic tendency do not as a rule occur in chronic granulocytic leukemia until the disease is far advanced Isolated hemorrhages may however occur relatively early in the course of the illness and may be due to leukemic vascular infiltration In the late stages bleeding is due chiefly to thrombocytopenia and generalized capillary damage Thrombotic manifestations include priapism a relatively rare development, but one which is extremely painful and may be the patient's presenting complaint

On examination, the patient with early or moderately advanced chronic granulocytic leukemia often appears healthy and well-nourished although he is frequently apprehensive and nervous and there may be evidence of recent weight loss Pallor of the mucous membranes may be apparent although the face is often flushed The advanced stage of the disease is characterized by progressive emaciation extreme pallor and prominence of the abdomen due to the enlarged spleen and liver Skin lesions are not common in chronic granulocytic leukemia but sometimes are a striking feature of the disease, and are of serious prognostic import They may appear as asymptomatic brown or bluish pinhead to walnut sized raised or flattened circumscribed infiltrations in the skin or subcutaneous tissues Occasionally discrete tumors as large as a golf ball project from the surface of the body and tend to become ulcerated with secondary infection and necrosis Tenderness of the sternum often localized to a small area is present in the majority of patients with chronic granulocytic leukemia

Splenic enlargement usually with preservation of the normal contour of the organ is almost always demonstrable even in patients seen during the earliest recognizable period of the disease Splenomegaly tends to increase with progression of the illness but there is no close correlation between spleen size and clinical course or hematologic changes Enlargement of the liver due to leukemia-cell infiltration is common in the more advanced stages of chronic granulocytic leukemia On the other hand peripheral lymph node enlargement usually is present to only slight degree even in far-advanced chronic granulocytic leukemia

Although not common early in the disease a variety of manifestations due to localized tissue infiltration may be present in chronic granulocytic leukemia These include visual disturbances caused by retinal hemorrhages leukemic retinitis throm

Henshaw and Hawkins state that in 1939–40 leukemia accounted for 3 6 per cent of all deaths due to cancer A number of reports indicate that the incidence of leukemia found at necropsy in general hospitals is slightly less than 1 per cent

Highly suggestive although not conclusive evidence indicates that the true incidence of leukemia is increasing, especially the acute forms of the disease in the younger age groups

*Etiologic Considerations* —As has already been indicated leukemia is generally believed to be a malignant neoplasm In the fourth edition of the *Standard Nomenclature of Disease* leukemia is classified as a new growth affecting specialized mesenchymatous tissue A number of contributory or provocative factors have been presumed to influence the development of leukemia These factors include heredity occupation infection, trauma, and chemical and physical agents

There is no evidence that leukemia is an hereditary disease in the sense of gene transmission On the other hand, an increased incidence of leukemia, particularly the lymphocytic variety in certain families is clearly indicated by numerous reports Congenital leukemia, most often the granulocytic form, has been reported as a rare but well authenticated occurrence It is not unusual for women with chronic leukemia to carry pregnancy to term but there is no recorded instance of congenital leukemia when either parent had the disease

With respect to occupation the recognized incidence of leukemia in physicians is 1 7 times that in the adult white male population and the disease has occurred in radiologists eight to ten times more frequently than in nonradiologists

The theory of an infectious cause for leukemia has received wide credence The nature of the leukocyte changes in leukemia may resemble those observed in known infectious conditions with either neutrophilic or lymphocytic reactions The clinical features of the rapidly progressive forms of leukemia—including fever of "septic" type sweating and the appearance of extreme "toxicity" — simulate those of acute severe infection The chronological relationship between a known infection such as one of the acute exanthemata and the clinical onset of acute leukemia has been noted so frequently as to suggest more than coincidence However, claims for a specific bacteriologic causative agent in leukemia have never been substantiated and there is no evidence of transmissibility of leukemia in man Mammalian leukemia may be transmitted in susceptible inbred strains of animals by inoculation of living cells Fowl leukemia may be transferred from an affected to a healthy bird by means of a cell free Berkefeld filtered tissue extract indicating a viral etiology for this form of the disease Although it appears extremely unlikely that mammalian leukemia is caused by specific infective agents the possible provocative role of infection in inducing leukemia in susceptible individuals is a plausible concept

Leukemia becoming manifest after trauma, especially abdominal injuries and fractures, has received considerable attention in the literature and may have medico legal significance There is no convincing evidence that the leukemia in such instances usually of the chronic granulocytic variety, was not present before the injury

Irradiation, as a physical agent responsible for the development of leukemia, has already received attention in connection with the reported higher incidence of the disease among radiologists The incidence of spontaneous leukemia in susceptible strains of mice has been greatly increased by exposing the animals to gamma radiation or *x* rays

Cases have been reported incriminating many chemicals including therapeutic agents and industrial intoxicants as causes of isolated instances of leukemia With the possible exception of benzol the etiologic role of these compounds in human leukemia is extremely dubious On the other hand it has been well established that carcinogenic agents such as benzpyrene and methylcholanthrene may induce leukemia in experimental animals

*Clinical Manifestations of Leukemia in General* —The symptoms and signs of leukemia are extremely varied and there is wide divergence between the features of chronic leukemias and those of the acute forms of the disease Nevertheless the most common clinical manifestations of all

greater numbers of immature granulocytes particularly myeloblasts and progranulocytes, in the circulating blood and by the development of thrombocytopenia Death is usually due to a cerebro vascular accident generalized bleeding or intercurrent infection with emaciation fever and anemia as contributory factors

## CHRONIC LYMPHOCYTIC LEUKEMIA

(LYMPHATIC LYMPHOGENOUS LEUKEMIA)

As mentioned earlier chronic lymphocytic leukemia tends to occur in an older age group and has a greater predilection for the male sex than is the case with chronic granulocytic leukemia The disease is extremely variable in its symptomatology and course and may remain in an asymptomatic and nonprogressive phase for years As in chronic granulocytic leukemia there may be manifestations due to pressure exerted by leukemic tumors anemia hypermetabolism and leukemic-cell tissue infiltration but in the lymphocytic form of the disease tendency to hemorrhage susceptibility to pulmonary infection and a high incidence of cutaneous manifestations are relatively early and prominent feature

On physical examination the distinguishing feature of chronic lymphocytic leukemia is characteristically bilateral symmetrical enlargement of cervical axillary and inguinal lymph nodes All lymphocytic tissues tend to become involved including medi astinal intra abdominal and retroperitoneal nodes and the spleen The peripheral tumors are of a firm rubbery consistency discrete freely movable and nontender Although occasionally they are as large as baseballs they range more commonly from pea to walnut size Rarely no palpable lymphadenopathy is demonstrable Splenomegaly although usually present is seldom of the degree characteristically associated with chronic granulocytic leukemia Sometimes however in advanced stages of the disease it attains enormous size

The cutaneous lesions may be lymphocytic infiltrations leukemic in nature or non specific secondary skin conditions called *leukemids* The latter may be vesicular urticarial, pustular or hemorrhagic and are often pruritic Both herpes simplex and herpes zoster occur frequently in chronic lymphocytic leukemia

*Hematologic Examination* —In the typical case of chronic lymphocytic leukemia diagnosis is readily made by a glance at the stained blood film The great number of lymphocytes exhibiting striking uniformity in size and staining properties serves at once to identify the nature of the disorder The total leukocyte count is exceedingly variable and although the level is usually in excess of 50 000 cells per cu mm when the patient is first seen subleukemic and aleukemic forms of chronic lymphocytic leukemia are not uncommon On the other hand very high counts counts exceeding 1 000 000 per cu mm , are sometimes observed With progression of the disease greater variations in the character of the lymphocytes occur and increasing numbers of prolymphocytes (inter mediate between lymphoblasts and mature lymphocytes) appear in the circulating blood

Anemia tends to develop later in the course of chronic lymphocytic leukemia than in that of the granulocytic form of the disease When present it is almost always associated with thrombocytopenia In advanced but not necessarily the terminal stages when myelopoiesis is almost completely replaced by proliferating lymphocytes there may be virtually no production of erythrocytes granulocytes or thrombocytes Occasionally secondary or symptomatic hemolytic anemia develops relatively early in the course of chronic lymphocytic leukemia Its recognition is of importance since with appropriate therapy which may include splenectomy the hemolysis can usually be corrected

Bone marrow examination aside from its diagnostic value in subleukemic and aleukemic forms of chronic lymphocytic leukemia is of considerable importance in evaluating the extent of normal myeloid replacement by leukemic cells

*Prognosis* —Although the average duration of life after the onset of symptoms is almost the same in both chronic lymphocytic and granulocytic leukemia—namely about $3\frac{1}{2}$ years the range is much wider in the

bosis of the central retinal vein, optic atrophy, or papilledema Deafness, tinnitus and vertigo may result from involvement of the auditory nerve or the labyrinth Cerebral hemorrhage or thrombosis may lead to hemiplegia Infiltration of nervous tissue by leukemic cells or pressure exerted by cellular proliferation may produce neurologic signs Involvement of skeletal structures causes pain, limitation of motion, pathologic fractures and sometimes transverse myelitis Similarly, other systems may be affected giving rise to a wide variety of clinical manifestations

*Hematologic Examination* —The leukemic form of chronic granulocytic leukemia is *much more common than the subleukemic* or aleukemic varieties When a patient first presents himself with symptoms referable to the disease there is almost invariably moderate or severe anemia The leukocyte count is usually between 100,000 and 300 000 per cu mm and occasionally the value exceeds 500 000 Immature granulocytes are always present and neutrophilic myelocytes and metamyelocytes usually account for 20 to 50 per cent of the *circulating white corpuscles* The *remainder* of the leukocytes are predominantly band and segmented neutrophils but there is characteristically an increase in eosinophilic and basophilic elements including immature forms Myeloblasts are almost always present in the blood but until the process is well advanced their number is relatively small and rarely exceeds 5 per cent in the differential count With progression of the disease to its terminal phase the majority of the white corpuscles become atypical myeloblasts and progranulocytes (promyelocytes with nonspecific cytoplasmic granulation)

The anemia is characteristically normocytic and normochromic except when there is an associated iron *deficiency giving rise* to microcytosis and hypochromia Moderate anisocytosis and polychromasia stippling and occasional nucleated erythrocytes are commonly observed on the stained blood films and there is usually a slight increase in reticulocyte numbers These changes may be present very early in the course of the disease when there is little or no anemia As the condition progresses, frequent transfusions may be required in order to maintain hemoglobin levels compatible with life

The thrombocytes in chronic granulocytic leukemia are usually normal or increased in *number until the disease is far advanced* when profound thrombocytopenia may develop In some cases extremely high thrombocyte counts, exceeding 1 000 000 per cu mm are observed, affording evidence of megakaryocytic involvement in the leukemic process Not infrequently, megakaryocyte fragments are observed in the circulating blood and many of the thrombocytes are large and of bizarre shape The increased number of platelets may be a *factor in thrombus formation*

Bone marrow examination is rarely necessary and is not particularly helpful in the diagnosis of chronic granulocytic leukemia The marrow is diffusely hyperplastic, with relative and absolute increase in granulocytic elements and numerous megakaryocytes Except for heightened activity the maturation of the cells does not appear to be grossly disturbed until in the late stages blast cell proliferation with little differentiation, supervenes *In some cases* abnormalities of erythropoiesis may be apparent characterized by numerous atypical rubriblasts (proerythroblasts) and prorubricytes (early normoblasts)

*Prognosis* —Although the course of chronic granulocytic leukemia may be favorably modified by judicious therapy as a rule treatment has little effect on duration of life Survival after onset of symptoms averages slightly more than three years with great individual variation It is probable that the disease is present in the asymptomatic phase for at least a year Few patients live longer than five years after the diagnosis is made although instances are on record of survival for as long as sixteen years

The duration of life is not correlated with age or sex nor in leukemic cases with the total leukocyte count at the time of diagnosis The course is usually more rapid in patients with the subleukemic form of the *disease* Severe *anemia is an unfavorable sign* *Progression is indicated by decreasing* periods of improvement after therapy by

forms with abundant pale-blue staining cytoplasm containing azurophilic granulation and irregularly shaped nuclei often folded, with a fine net like arrangement of chromatin and small indistinct nucleoli Progressive normocytic normochromic anemia and extreme thrombocytopenia develop early in the course of monocytic leukemia

Bone marrow examination is an essential diagnostic procedure in the subleukemic and aleukemic forms of normocytic leukemia and is of great value in the differentiation of the myelomonocytic and histiomonocytic varieties

## ACUTE LEUKEMIAS

Because of the similarities in clinical manifestations exhibited by the various types of acute leukemia and because identification of the cell series involved in the leukemic process may be difficult it is convenient to consider these entities together The subdivision of the rapidly progressive forms of leukemia into acute and subacute groups is objected to by many as arbitrary and without well-defined criteria of differentiation Nevertheless the distinction appears to serve a useful purpose particularly in evaluating the effects of therapeutic measures which have been recently introduced for the treatment of these disorders In the group classified as acute the patient is severely ill virtually from the time of onset of the first symptom In the subacute group the progress of the disease is more insidious and there is more likelihood of its therapeutic modification Nevertheless the clinical and hematologic features are the same except in degree for the two subdivisions

Of a series of 495 cases of leukemia observed at the Simpson Memorial Institute of the University of Michigan between 1927 and 1940 a total of 168 or 33 9 per cent were classified as acute (including subacute) The incidence of the various types of acute leukemia was as follows

| | *Per Cent* |
|---|---|
| Acute granulocytic (including acute myelomonocytic and hemocytoblastic) | 50 0 |
| Acute lymphocytic | 34 5 |
| Acute monocytic (histiomonocytic only) | 15 5 |

Acute lymphocytic leukemia occurs predominantly in children whereas the granulocytic and monocytic forms of the disease are most common in young adults The latter conditions however may affect persons of advanced age

*Symptoms and Signs* —After an initial period of varying length during which there may be vague symptoms of ill health the course is generally rapid and progressive and resembles that of a severe septic process complicated by hemorrhagic manifestations and severe anemia Pain referred to the bones and joints is not uncommon especially in children Rarely temporary remissions may interrupt the progress of the disease and these may follow an acute infection or the administration of blood transfusions

Physical signs except for fever pallor and hemorrhage including purpura and bleeding from the orifices of the body are not so striking in acute as in chronic leukemias Lymph node enlargement and splenomegaly are usually present but of slight or moderate degree Infection of the oropharynx is common Manifestations due to leukemic-cell infiltration of systems other than the hemic and lymphatic may occur but they are rare in acute leukemia Death is usually due to prostration and toxemia unless the course of the illness has been modified by specific therapy Hemorrhage and intercurrent infection are common terminal events

*Hematologic Examination* —At the time of diagnosis the leukocyte count is usually moderately elevated However almost as frequently the value is either within normal limits or definitely leukopenic Counts above 100 000 per cu mm are uncommon although in acute lymphocytic leukemia there may be a terminal increase to very high levels Immature cells are always present in the circulating blood at some time during the course of the disease but their number may fluctuate widely Usually the majority of the cells are in the blast or prostage of development Their appearance may differ greatly from that of the corresponding elements present in normal marrow or lymph tissue Disparity between nuclear and cytoplasmic development great

former It is believed that this variation is attributable in part to the usual inclusion with chronic lymphocytic leukemia of cases of disseminated lymphosarcoma with blood stream invasion Although this condition is properly classified as a variant of lymphocytic leukemia its course is generally more rapid than that of the typical chronic form of the disease In a series of 61 cases diagnosed as lymphosarcoma cell leukemia the average duration of life after the onset of symptoms was 31 months In the same report the length of survival of 33 cases of typical chronic lymphocytic leukemia was found to be 58 months Many patients live longer than ten years after the diagnosis of chronic lymphocytic leukemia, and their number has constantly increased since the advent of effective measures for combatting *intercurrent infection* Formerly *infection* usually pneumonia was the commonest cause of death in patients with chronic lymphocytic leukemia At present hemorrhage and anemia account for the greatest *number of deaths but, in the older* age groups especially there is a strong possibility that the patient will succumb to a condition unrelated to his leukemia

## *MONOCYTIC LEUKEMIA*

Monocytic leukemia although a recognized entity, is less well defined both clinically and hematologically and its incidence is much lower than either granulocytic or lymphocytic leukemia The course of the disease is usually rapid and the clinical features are in general those characteristic of the acute and subacute forms of leukemia The great majority of patients with monocytic leukemia die within six months of the onset of symptoms the average survival period being about three months Rarely the course of the illness is protracted over a period of years and it has been thought that such cases may *evolve from* a form of non malignant reticulo-endotheliosis

Patients with monocytic leukemia are especially prone to develop lesions of the skin and mucous membranes Gingival hyperplasia with infection and hemorrhage is a common occurrence Cutaneous involvement is most likely to occur over the face and trunk and may take the form of diffuse papules or isolated nodules Secondary bacterial invasion is common leading to the formation of indolent pustules furuncles, or carbuncles These lesions usually have a distinctive violaceous coloration and they may break down to form shallow ulcers Infection of the gingivae tends to extend to the oropharynx leading to necrosis and gangrene Much may be accomplished toward the prevention of these distressing manifestations by a rigid program of oral hygiene and by the local and systemic use of antibiotics with wide spectra of activity

Enlargement of lymph nodes and spleen is not usually a conspicuous feature of monocytic leukemia, and may be absent throughout the course of the illness On *the other hand, hepatomegaly is a relatively* common and prominent manifestation Progression of the disease is characterized by irregular fever generalized bleeding and increasingly severe anemia

*Hematologic Examination* —*Based upon* the supposed origin of the leukemic cells two types of monocytic leukemia are recognized One bearing a close relationship to the granulocytic series of the bone marrow has been termed the *Naegeli type* or *myelomonocytic* leukemia and may be considered a variant of the granulocytic form of the disease The other type which appears to arise directly from the reticulo-endothelial or histiocytic tissue has been designated the *Schilling type* or *histiomonocytic* leukemia and is believed by some to constitute the only true monocytic leukemia

The leukocyte count in monocytic leukemia rarely exceeds 100 000 cells per cu mm and is usually below *50 000* Subleukemic forms of the disease are common but as in all varieties of subleukemic and aleukemic leukemia the peripheral blood picture may change during the evolution of the disease and become frankly leukemic Cells of the monocytic series constitute a variable percentage of the circulating leukocytes the usual range being between 50 per cent and 80 per cent All stages of cellular differentiation are usually represented including blast forms promonocytes and mature *monocytes* as well as both large histiocytic

The nitrogen mustards in particular methyl bis (β chloroethyl) amine hydrochloride, have an inhibitory effect on leukemic cell proliferation The usual dosage of this compound is 0 4 mgm per kilogram of body weight given intravenously in four divided doses at daily or two-day intervals A maximum of 24 mgm in a single course of four doses is advised, and courses of therapy ordinarily should not be repeated more often than every six weeks Nitrogen mustard has a limited field of usefulness in the treatment of chronic leukemia and is contraindicated in the acute form of the disease Its therapeutic effect is induced more rapidly but is of shorter duration than that following irradiation Consequently its greatest value is in the relief of pain pressure manifestations and symptoms of hypermetabolism in patients with terminal chronic leukemia A recently introduced therapeutic agent triethylene melamine (T E M ) is said to have the same pharmacologic action as the nitrogen mustards It may be given orally and does not produce the severe nausea and vomiting which usually follows nitrogen mustard administration The recommended dose is 5 mgm daily until a decrease in the leukocyte count is observed Thereafter the drug should be administered cautiously and in amounts not greater than 5 mgm every second day Both nitrogen mustard and triethylene melamine are powerful myeloid depressants and may induce profound granulocytopenia and thrombocytopenia

Urethane (ethyl carbamate) was introduced in 1946 for the treatment of leukemia Its value is limited essentially to the management of relatively early cases of chronic leukemia particularly the granulocytic variety and its chief application is to cases in which irradiation therapy is impractical The usual dosage at the outset of therapy is from 3 to 4 grams daily in the form of enteric-coated tablets or in solution in a syrupy vehicle Maintenance therapy, employing a reduced dosage of from 1 5 to 2 grams daily may be carried out Gastric intolerance may prevent continued use of urethane and patients receiving the drug should be kept under observation for development of severe leukopenia Transiently favorable effects have followed the administration of urethane in some cases of monocytic leukemia

Arsenic usually employed in the form of solution of potassium arsenite (Fowler s solution), is the oldest agent still in use for the treatment of leukemia It is effective in many chronic cases especially before the disease becomes well advanced but it is generally inferior to other available therapeutic measures In order to obtain the desired results it is usually necessary to increase the drug to the limit of tolerance thereby provoking undesirable side effects including gastrointestinal disturbances weight loss and skin eruptions with pruritus and pigmentation

Until the introduction of the folic acid antagonists and more recently adrenocorticotropic hormone (ACTH) and cortisone there were no specific measures available for the treatment of acute leukemia The rationale for the use of the folic acid antagonists is based upon the observations that folic acid is required for normal hemopoiesis and that rapidly proliferating leukemic cells contain more of the vitamin than do normal cells By inducing a deficiency of folic acid the growth of blood cells and especially leukemic cells is inhibited and in some cases, the supression of leukemic-cell growth enables the body to restore temporarily and in varying degrees normal functional cellular differentiation Unfortunately, the margin between the desired effect on leukemic cells and the accompanying suppression of normal hemopoiesis is narrow and furthermore the widespread metabolic function of folic acid is reflected by serious toxic manifestations when folic acid antagonist therapy is employed The antagonists are chemical analogues of folic (pteroylglutamic) acid and the most powerful and most widely used of this group of compounds is aminopterin (4 amino pteroylglutamic acid) Significant clinical improvement at times virtually complete, but temporary hematologic and clinical remission occurs in about 50 per cent of the children with acute leukemia treated with folic acid antagonists The percentage of adult patients who derive appreciable benefit from antagonist therapy is much smaller Toxic manifestations in

variation in cell size, relatively large nuclei and prominent nucleoli are commonly observed features of leukemic cells

Anemia and thrombocytopenia are almost always present at the time of initial examination of a patient with acute leukemia In the more fulminating cases with little or no production of functional myeloid elements, the shorter life span of the platelets as compared to that of the erythrocytes may lead to profound thrombocytopenia before the development of a significant degree of anemia Such cases have been mistakenly diagnosed as acute idiopathic thrombocytopenic purpura

Bone marrow aspiration aids in distinguishing between the several types of acute leukemia and in subleukemic cases, may be essential to the diagnosis

### Treatment of Leukemia

Roentgen irradiation is the most valuable therapeutic agent available for the management of patients with chronic leukemia This form of treatment first employed by Pusey in 1902, has been applied according to a variety of techniques In general, two points of view have governed the use of irradiation therapy According to one, treatment should be reserved until the disease is manifestly active and should then be applied close to the limit of tolerance The second view which is gaining increasing favor, holds that the aim of treatment should be to maintain the patient in as complete clinical and hematologic remission as possible by the administration of therapy as often as necessary, until the terminal phase of the illness Such a program, employing periodic relatively small doses of irradiation, serves to avoid severe postirradiation sickness and depression and enables the patient to lead an essentially normal life throughout the greater part of his illness Achievement of this objective depends upon close cooperation of the internist and radiotherapist and requires frequent careful clinical and hematologic evaluation of the patient s status

Deep $x$ ray therapy may be applied, in a course of small doses to the entire body with the face and genitalia shielded or may be administered more intensively to a series of localized fields, such as peripheral nodes mediastinum, retroperitoneal region and spleen Choice of the method employed should be governed by the situation presented by the individual patient In general, total body irradiation is preferable during the earlier phases of both chronic granulocytic and lymphocytic leukemia in the absence of great enlargement of the spleen or lymph nodes Local irradiation should be employed for the relief of pressure manifestations or pain due to leukemic cell infiltration and for the reduction of greatly enlarged peripheral lymph nodes

X ray therapy is of no value in monocytic leukemia except in the treatment of local lesions, and its use in acute leukemia is likely to be followed by an enhanced activity of the process Less favorable effects are usually obtained in subleukemic and aleukemic granulocytic and lymphocytic leukemia than in the definitely leukemic form of these diseases Irradiation should be given with caution in the presence of severe anemia or thrombocytopenia a rapid decline in the leukocyte count is an indication for the discontinuance of a course of therapy

Radioactive isotopes and in particular, the isotope of phosphorus $P_{32}$ have been employed for the treatment of chronic leukemia in an increasing number of medical centers since the first report of the use of $P_{32}$ for this purpose by Lawrence in 1940 Radioactive phosphorus offers a convenient means of obtaining widespread irradiation of tissue Its advantages, which are more theoretical than proved depend upon its selectively greater deposition in rapidly proliferating cells its emission of high energy beta rays absorbed within a few millimeters of their point of origin, and its radiation half life of 14 3 days which permits prolonged and if desired continuous irradiation In addition the administration of $P_{32}$ is followed by little or no radiation sickness

The indications and limitations for the use of $P_{32}$ are the same as those for total body roentgen irradiation and there is no convincing evidence that the therapeutic results obtained by its administration are superior to those of $x$ ray therapy

tion It is characterized by diffuse myeloma cell infiltration of the bone marrow and local tumor formation in the bone marrow (this resulting in bone destruction and anemia) by myeloma cell invasion of nonskeletal tissues, hyperglobulinemia and by the frequent presence of a peculiar type of protein in the urine (Bence Jones proteinuria) Plasmocytic myeloma is closely related to the leukemias and may in fact be designated as aleukemic subleukemic or leukemic plasmocytic leukemia depending upon the presence of plasmocytes in the circulating blood

No reliable statistics on the true incidence of plasmocytic myeloma are available Formerly considered a rare disease it is now recognized much more frequently due to the wider use of sternal aspiration in the diagnosis of obscure cases of progressive anemia skeletal pain and osseous lesions The onset of symptoms usually occurs after the age of 40 although instances of the disease have been reported in children Males are affected at least twice as frequently as females

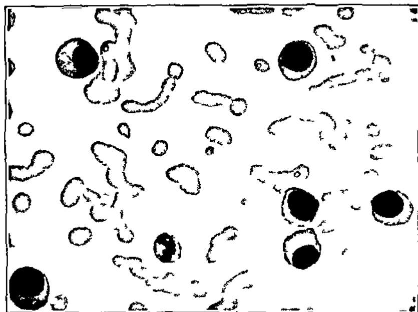


FIG 191 —Photomicrograph showing myeloma cells in material obtained by sternal puncture in a case of multiple myeloma The eccentricity of the nuclei is well shown and the dark ground glass vacuolated cytoplasm is evident (Wintrobe s Clinical Hematology )

Symptoms of anemia weight loss pains in the back or at the site of a pathologic fracture are the most common presenting complaints Physical findings are usually noncontributory, although bone tenderness may be elicited

The liver is often enlarged but the spleen is seldom palpable Roentgenographic examination may reveal the characteristic discrete punched-out osteolytic lesions especially in the skull ribs and pelvic bones Sometimes however the findings are limited to generalized osteoporosis and in some instances the skeletal survey yields negative results

Extra-osseous tissue invasion by myeloma cells is commonly observed at necropsy, but such involvement rarely gives rise to localizing signs Renal insufficiency frequently develops during the course of plasmocytic myeloma and is probably caused by precipitation of abnormal globulins in the tubules Death may be due to kidney failure with uremia

*Laboratory Findings* —Examination of the peripheral blood may reveal no significant abnormalities More commonly there is

addition to granulocytopenia and thrombocytopenia, are referable chiefly to the alimentary tract and include aphthous lesions of the oropharynx and ulceration with hemorrhage of the esophageal gastric, and intestinal mucosa Epilation is a common sequel of antagonist therapy The usual dosage of aminopterin is from 0.5 to 1.0 mgm daily, given either orally or parenterally until an effect is obtained Subsequent administration depends upon individual indications It should be emphasized that folic acid antagonist therapy *is hazardous and its use justified only by the* desperate nature of the illness it is designed to combat

Encouraging early reports of the effects of ACTH and cortisone in cases of acute leukemia have not been substantiated by greater experience in the use of these hormones It is undoubtedly true that the adrenal cortex is concerned with the maintenance of the hemic equilibrium and its stimulation by ACTH or the use of substitution therapy, tends to suppress lymphocytic hyperplasia and promote myeloid cell proliferation and functional differentiation Nevertheless beneficial results of adrenocortical therapy in acute leukemia although sometimes striking are extremely transitory The combined or alternate use of folic acid antagonist and adrenocortical therapy is worthy of consideration in selected cases of acute leukemia

ACTH and cortisone have been advocated for the treatment of chronic lymphocytic leukemia between courses of irradiation Its value in such cases has not been fully determined but it seems to be established that patients with long standing slowly progressive malignant lymphoma may derive benefit from adrenocortical therapy and that the pruritus frequently associated with such disorders may be substantially relieved

## REFERENCES


BETHELL F H Lymphogenous (Lymphatic) Leukemia J A M A, 1942 *118* 95

———— Leukemia The Relative Incidence of Its Various Forms and Their Response to Radiation Therapy Ann *Int Med* 1943 *18* 757

Committee for Clarification of the Nomenclature of Cells and Diseases of the Blood and Blood Forming Organs Third Fourth and Fifth Reports Am J Clin Path 1950 *20* 562

COOPER T and WATKINS C H Ethyl Carbamate (Urethane) in the Treatment of Chronic Myelocytic Leukemia Results of a Three Year Study M Clin North America 1950 *34* 1205

DAMESHEK W FREEDMAN M H and STEINBERG I Folic Acid Antagonists in the Treatment of Acute and Subacute Leukemia Blood 1950 *5* 898

EVANS T S Monocytic Leukemia Medicine 1942 *21* 421

FARBER S Some Observations on the Effect of *Folic Acid Antagonists on Acute Leukemia and* Other Forms of Incurable Cancer Blood 1949 *4* 160

LOW BEER B V A LAWRENCE J H and STONE R S The Therapeutic Use of Artificially Produced Radioactive Substances Radiology 1942 *39* 573

MARCH H C Leukemia in Radiologists in a 20 Year Period Am J M Sc 1950 *220* 282

MINOT G R BUCKMAN T F and ISAACS R Chronic Myelogenous Leukemia Age Incidence Duration and Benefit Derived from Irradiation Jour Am Med A sn 1924 *82* 1489

MINOT G R and ISAACS R Lymphatic Leukemia Age Incidence Duration and Benefit Derived from Irradiation Boston Med and Surg Jour 1924 *191* 1

REINHARD E H MOORE C V BIERBAUM O S and MOORE S Radioactive Phosphorus as a Therapeutic Agent Jour Lab and Clin Med 1946 *31* 107

SPURR C L SMITH T R BLOCK M and JACOBSON L O The Rôle of Nitrogen Mustard Therapy in the Treatment of Lymphomas and Leukemias Am J Med 1950 *8* 710

STICKNEY J M HECK F J and WATKINS C H Cortisone and ACTH in the Management of Leukemia and Lymphoblastoma Proc Staff Meet Mayo Clin 1950 *25* 488

ULRICH H The Incidence of Leukemia in Radiologists New England Jour Med 1946 *234* 45

WATKINS C H COOPER T and GIFFIN H Z The Use of Urethane (Ethyl Carbamate) in the Treatment of Leukemia Blood 1948 *3* 892

WINTROBE M M and HASENBUSH L L Chronic Leukemia Arch Int Med 1939 *64* 701


## PLASMOCYTIC MYELOMA
### (MULTIPLE MYELOMA)

BY FRANK H BETHEL M D

Plasmocytic myeloma is a neoplastic disease of mesenchymatous tissue exhibiting varying degrees of plasmocytic differentia

tion It is characterized by diffuse myeloma cell infiltration of the bone marrow and local tumor formation in the bone marrow (this resulting in bone destruction and anemia) by myeloma-cell invasion of nonskeletal tissues hyperglobulinemia and by the frequent presence of a peculiar type of protein in the urine (Bence-Jones proteinuria) Plasmocytic myeloma is closely related to the leukemias and may in fact be designated as aleukemic subleukemic or leukemic plasmocytic leukemia depending upon the presence of plasmocytes in the circulating blood

No reliable statistics on the true incidence of plasmocytic myeloma are available Formerly considered a rare disease it is now recognized much more frequently due to the wider use of sternal aspiration in the diagnosis of obscure cases of progressive anemia skeletal pain and osseous lesions The onset of symptoms usually occurs after the age of 40 although instances of the disease have been reported in children Males are affected at least twice as frequently as females

Symptoms of anemia weight loss pains in the back or at the site of a pathologic fracture are the most common presenting complaints Physical findings are usually noncontributory although bone tenderness may be elicited

The liver is often enlarged but the spleen is seldom palpable Roentgenographic examination may reveal the characteristic discrete punched-out osteolytic lesions especially in the skull ribs and pelvic bones Sometimes however the findings are limited to generalized osteoporosis and in some instances the skeletal survey yields negative results

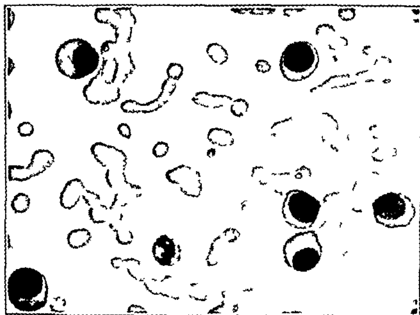


Fig 191 —Photomicrograph showing myeloma cells in material obtained by sternal puncture in a case of multiple myeloma The eccentricity of the nuclei is well shown and the dark ground glass vacuolated cytoplasm is evident (Wintrobe s Clinical Hematology )

Extra-osseous tissue invasion by myeloma cells is commonly observed at necropsy but such involvement rarely gives rise to localizing signs Renal insufficiency frequently develops during the course of plasmocytic myeloma and is probably caused by precipitation of abnormal globulins in the tubules Death may be due to kidney failure with uremia

*Laboratory Findings* —Examination of the peripheral blood may reveal no significant abnormalities More commonly there is

moderate normochromic normocytic or slightly macrocytic anemia. Sometimes the anemia is severe with a hemoglobin value of less than 5 grams per 100 cc. Usually, the leukocyte count is within the normal range or the value is slightly leukopenic, and the differential count is within normal limits. Plasmocytes are not infrequently present. Their detection may require careful search, or they may constitute an appreciable percentage of the total leukocyte number. Very rarely, the picture may be that of true plasmocytic leukemia. Thrombocytes are commonly reduced in number and are usually within the range of from 100 000 to 200 000 per cu mm. Occasionally thrombocytopenia may be of such severity as to cause hemorrhage. A noteworthy feature of the stained blood film is the frequent occurrence of tightly clumped aggregates of erythrocytes. These may appear against a lightly tinted background of dried plasma. Such changes are presumably caused by hyperglobulinemia.

Bence-Jones proteinuria is demonstrable in approximately 65 per cent of the cases of plasmocytic myeloma, although the detection of this abnormal protein in the urine of an individual patient may require repeated examination. Albuminuria and other evidences of renal pathology are frequently observed.

Blood chemical changes commonly but not invariably, occurring in plasmocytic myeloma include the hyperglobulinemia which may exceed 10 grams per 100 cc and an increased level of serum calcium usually within the range of 12 to 16 mgm per 100 cc. As a rule the inorganic serum-phosphorus value is within normal limits. The nonprotein nitrogen and creatinine levels of the serum may be elevated in the presence of renal impairment.

Aspiration of bone marrow from the sternum iliac crest or vertebral spinous process usually serves to establish a cytologic diagnosis in patients with plasmocytic myeloma. Quantitatively, the marrow appearance may vary from almost complete replacement of granulocytic and erythrocytic elements by plasmocytes to the finding of occasional scattered myeloma cells among normally developing myeloid elements. Repeated aspiration is sometimes necessary before conclusive evidence of the disease is secured and rarely biopsy of a localized lesion is required in order to arrive at the diagnosis. Qualitatively, the myeloma cells may have the appearance of extremely primitive forms (plasmoblasts) or may exhibit evidence of increasing degrees of differentiation (proplasmocytes and plasmocytes).

*Prognosis* —Plasmocytic myeloma is usually a slowly progressive disease, death ensuing within two years after the onset of symptoms. Its course may be modified and symptoms relieved by appropriate therapy but therapeutically induced remissions of the type commonly observed in chronic granulocytic and lymphocytic leukemia rarely occur in plasmocytic myeloma. Occasionally however, the disease appears to enter a spontaneous remission and instances of long survival are on record. Death is usually due to cachexia, anemia hemorrhage intercurrent infection (especially pneumonia) or the complications of pathologic fractures, including transverse myelitis.

*Treatment* —Roentgen irradiation to localized regions of involvement may relieve pain especially of radicular origin. Radioactive phosphorus is of limited value but may provide remarkable palliation of symptoms in advanced cases. Stilbamidine has been advocated for this purpose. ACTH or cortisone administration may be followed by considerable subjective improvement and in some cases by increase in erythrocytic values and reduction in plasma globulin. The effect of these hormones however is usually brief. Urethane has been found to be of considerable value in the management of many patients with plasmocytic myeloma. The dosage should be raised to the limit of gastric tolerance usually the dose is 4 0 grams daily given in divided doses with close observation in order to avoid severe toxic marrow depression or hepatic damage.

*Plasmocytic Leukemia* —Occasional plasmocytes are noted in films of the circulating blood in many cases of plasmocytic leukemia. It is unusual for their number to be sufficiently large as to constitute an important

diagnostic aid Rarely however the blood picture may be frankly leukemic Counts in excess of 100 000 per cu mm consisting of more than 90% plasmoblasts proplasmocytes or plasmocytes have been reported When such changes are present the condition may be designated as *plasmocytic leukemia* either acute subacute or chronic depending upon the degree of immaturity of the predominating cells In general the course of the disease is more rapid and the response to therapy less favorable in plasmocytic leukemia than in the more localized myelomas

REFERENCES


BAYRD F D and HALL B E Unusual Remission after Radiophosphorus Therapy in a Case of Acute Plasma Cell Leukemia Blood 1948 *3* 1019

GESCHICKTER C F and COPELAND M M Multiple Myeloma Arch Surg 1928 *16* 807

GHORMLEY R K POLLOCK G A HALL B E and BEIZER L H Multiple Myeloma Surg Gynec & Obst 1942 *74* 242

LIMARZI L R PAUL J T and PONCHER H G Blood and Bone Marrow in Infectious Mononucleosis Jour Lab and Clin Med 1946 *31* 1079

LOGE J P and RUNDLES R W Urethane (Ethyl Carbamate) Therapy in Multiple Myeloma Blood 1949 *4* 201

PROPP S GORHAM L W and KANTOR S Recent Studies of Multiple Myeloma Sternal and Rib Puncture and the Results of Treatment with Stilbamidine Blood 1949 *4* 36

RUBINSTEIN M A Multiple Myeloma as a Form of Leukemia Blood *4* 1049 1949

SNAPPER I Stilbamidine and Pentamidine in Multiple Myeloma J A M A 1947 *133* 157


## INFECTIOUS MONONUCLEOSIS

### GLANDULAR FEVER ACUTE LYMPHADENOSIS

By FRANK H BETHEL M D

*Definition* —Infectious mononucleosis is an acute self limited infection presumably caused by a virus and characterized by fever sore throat and lymphadenopathy It is associated with a distinctive lymphocytic reaction and with the presence of circulating sheep-red-cell agglutinins (heterophil antibodies)

The disorder is a common infection of young persons and is especially prevalent among students Many cases undoubtedly are unrecognized The great majority of cases occur between the ages of 15 and 30 Young children may be affected but the disease is exceedingly rare after the age of 40 Males have the disorder more frequently than females in a ratio of 3 2 Although the disease is undoubtedly infectious with a usual incubation period between 5 and 15 days its order of contagiousness is apparently low Attempts to transmit the infection to human volunteers have met, at best with equivocal success

Typically the onset of infectious mononucleosis is manifested by upper respiratory symptoms and slight fever Headache and malaise are common The throat may be intensely sore The pharyngeal mucosa has a magenta tint rather than the bright erythema of a streptococcal infection Patches of grayish white exudate suggestive of a diphtheritic membrane may be present over the tonsils or pharyngeal lymph tissue Toward the end of the first week of illness sometimes later lymph nodes become enlarged and tender Those in the cervical and axillary regions are most frequently involved Rarely there is no demonstrable lymphadenopathy A transient cutaneous eruption usually macular or maculo-papular may occur during the early period of the illness Ocular manifestations including photophobia and conjunctivitis are not uncommon The spleen is palpable by the end of the second week in more than 50 per cent of cases The organ seldom is greatly enlarged but in rare instances it may be ruptured as the result of relatively slight trauma

Infectious mononucleosis is a generalized disease and there may be foci of mononuclear infiltration in the liver kidneys spleen nervous system and other tissues Such lesions may account for the varied clinical manifestations including the hepatic involvement with or without jaundice and the central nervous system manifestations which may occur during the course of the illness

*Hematologic Examination* —Infectious mononucleosis is a member of a group of diseases which characteristically induce a lymphocytic reaction Such reactions consist of proliferation of lymphocytic elements at varying stages of differentiation including the lymphoid reticulum Hyperplasia of

lymphocytic tissue is accompanied by a reciprocal suppression of granulocytic activity. In the early phase of infectious mononucleosis an interval lasting about a week, there is usually definite neutropenia *with relative lymphocytosis*. *During the* second week, coincident with lymph-node enlargement, the count rises and the characteristic mononuclear cells make their appearance in increasing numbers. These cells are derived from the lymphoid reticulum and vary greatly in their evidences of differentiation, as well as in size and shape. The majority of the mononuclear cells contain nuclei with irregularly massed deeply staining chromatin. The cytoplasm is abundant, has a foamy or vacuolated appearance and shows a tendency to stain more intensely at the periphery of the cell. A variable *number of the mononuclear elements*, usually a small percentage of the total, exhibit the characteristics of lymphoblasts. The nuclear chromatin is diffuse and stains lightly, nucleoli are discernible and the *cytoplasm may be quite scanty* and deeply basophilic. The presence of such cells is likely to suggest the diagnosis of acute lymphocytic leukemia. The leukocyte count may not rise above the normal range throughout the course of the illness but the usual peak is between 12,000 and 20,000 cells per cu mm. Rarely the value may exceed 40,000. Lymphocytes usually constitute between 50 and 80 per cent of the total number of leukocytes.

The erythrocytes and thrombocytes are ordinarily not affected in cases of infectious mononucleosis. However rare instances of associated thrombocytopenic purpura and of hemolytic anemia have been reported. Such complications may be attributed to reticulo-endothelial dysfunction and can probably be regarded as instances of secondary hypersplenism.

The bone marrow is infectious mononucleosis is not *significantly* abnormal and its examination is useful only in differential diagnosis when leukemia is suspected.

The heterophil antibody reaction of Paul and Bunnell which depends upon the agglutination of sheep red cells by antibodies in the patient's serum, has been found to be positive in about 90 per cent of the cases if tested for repeatedly throughout the first three weeks of the illness. A single negative test is of no diagnostic significance. A rising titer is of special diagnostic significance and the specificity of the test may be increased by absorption of the Forssman antibodies. A positive reaction may persist for several months after subsidence of the illness. Non-specific cold hemagglutinins may be present in the serum of patients with infectious mononucleosis and should be prevented from affecting the Paul Bunnell test. False positive serological reactions, for syphilis have been observed in from 10 to 20 per cent of the cases of infectious mononucleosis.

*Prognosis.*—The symptoms of acute illness generally subside within three weeks of the onset of fever in infectious mononucleosis. Lymphadenopathy and splenomegaly may *persist for several weeks or even months*. Return of the blood picture to normal usually coincides with regression of lymph node enlargement. Convalescence may be exceedingly protracted and characterized by ex*treme fatigability and lack of endurance*. Recrudescences of fever and lymphadenopathy occasionally occur. A few fatalities have been reported due to rupture of the spleen or to respiratory paralysis associated with the Guillain Barre syndrome.

*Treatment.*—No therapeutic agents including the more recently introduced antibiotics have been found to influence the course of infectious mononucleosis. They may be of value in controlling secondary bacterial infection particularly in the upper respiratory tract. Restriction of activity during the febrile period of the illness and symptomatic measures should be prescribed.

## REFERENCES


BERNSTEIN, A.: Infectious Mononucleosis. Medicine 1940, *19*, 85.

BERNSTEIN, T. C. and WOLFF, H. G.: Involvement *of the Nervous System in Infectious* Mononucleosis. Ann Int Med 1950, *33*, 1120.

DAVIDSOHN, I.: Serologic Diagnosis of *Infectious* Mononucleosis. Jour Am Med Assn 1937, *108*, 287.

EVANS, A. S.: Further Experimental Attempts to Transmit Infectious Mononucleosis to Man. Jour Clin Invest 1950, *29*, 508.

JORDAN, W. S., JR. and ALBRIGHT, R. W.: Liver Function Tests in Infectious Mononucleosis. Jour Lab and Clin Med 1950, *35*, 688.

Limarzi L R Paul J T and Poncher H G Blood and Bone Marrow in Infectious Mononucleosis Jour Lab and Clin Med 1946 *31* 1079

Lloyd P C Acute Thrombocytopenic Purpura in Infectious Mononucleosis Am Jour Med Sci 1944 *207* 620

Paul J R and Bunnell W W The Presence of Heterophile Antibodies in Infectious Mononucleosis Am Jour Med Sci 1932 *153* 90

Peterson R I Hepatic Dysfunction in Infectious Mononucleosis with Review of the Literature Jour Lab and Clin Med 1948 *33* 1258

Ricker W Blumberg A Peters C H and Widerman A The Association of the Guillain Barré Syndrome with Infectious Mononucleosis Blood 1947 *2* 217

Ziegler E E Infectious Mononucleosis Fatal Case with Autopsy Arch Path 1944 *37* 196

lymphocytic tissue is accompanied by a reciprocal suppression of granulocytic activity. In the early phase of infectious mononucleosis an interval lasting about a week there is usually definite neutropenia *with relative lymphocytosis*. *During the* second week coincident with lymph node enlargement, the count rises and the characteristic mononuclear cells make their appearance in increasing numbers. These cells are derived from the lymphoid reticulum and vary greatly in their evidences of differentiation as well as in size and shape. The majority of the mononuclear cells contain nuclei with irregularly massed deeply staining chromatin. The cytoplasm is abundant, has a foamy or vacuolated appearance, and shows a tendency to stain more intensely at the periphery of the cell. A variable number of the mononuclear elements, usually a small percentage of the total, exhibit the characteristics of lymphoblasts. The nuclear chromatin is diffuse and stains lightly, nucleoli are discernible and the cytoplasm may be quite scanty and deeply basophilic. The presence of such cells is likely to suggest the diagnosis of acute lymphocytic leukemia. The leukocyte count *may not rise above the normal range* throughout the course of the illness but the usual peak is between 12 000 and 20 000 cells per cu mm. Rarely the value may exceed 40 000. Lymphocytes usually constitute between 50 and 80 per cent of the total number of leukocytes.

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REFERENCES

BERNSTEIN A. Infectious Mononucleosis. Medicine 1940 *19* 85.

BERNSTEIN T C and WOLFF H G. Involvement *of the Nervous System in Infectious* Mononucleosis. Ann Int Med 1950 *33* 1120.

DAVIDSOHN I. Serologic Diagnosis of Infectious Mononucleosis. Jour Am Med Assn 1937 *108* 287.

EVANS A S. Further Experimental Attempts to Transmit Infectious Mononucleosis to Man. Jour Clin Invest 1950 *29* 508.

JORDAN W S JR and ALBRIGHT R W. Liver Function Tests in Infectious Mononucleosis. *Jour Lab and Clin Med* 1950 *35* 688.

megaly is important and often difficult The normal spleen though varying greatly in size in different individuals is practically never palpable and may be surprisingly enlarged without becoming so Its identification is aided by the outlinable dulness and characteristic notches on the lower margin Roentgen ray opacity may be accentuated Splenic puncture may reveal information of endocarditis (especially the latter) septicemia poliomyelitis brucellosis Weil s disease and epidemic hepatitis Oroya Malta trench and relapsing fever among the protozoan diseases to the malarias kala-azar Rocky Mountain spotted fever in chronic infections to syphilis tuberculosis to neoplasms and cysts and to some conditions of unknown etiology such as Boeck's sarcoid Mechanical

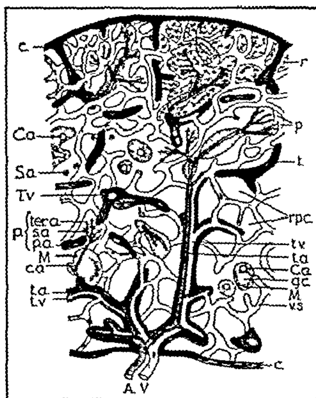



FIG 192 —Schema of the structure of the spleen *A* Artery entering at hilum *c* capsule *C a* central artery cross section *c a* central artery longitudinal section *g c* germinal center *M* Malpighian corpuscle *p* penicilli *p a* pulp artery *r* reticulum *r p c* red pulp cords *S a* sheathed artery in cross section *s a* sheathed artery longitudinal section *t* trabeculæ *t a* trabecular arteries *ter a* terminal arteries *t v* trabecular veins cross section *t v* trabecular veins longitudinal section V vein leaving at hilum *vs* venous sinuses (Courtesy of Bailey s Histology as modified from Hartmann )

value it is slowly coming into more frequent use *in this country* At present we believe that it should seldom be used because of *obvious hazards* and as the necessary information can usually be obtained by other means

Splenic enlargement beyond palpability may be due to such infections as typhoid and paratyphoid fevers infectious mononucleosis (up to 1 kg ) acute and subacute obstruction to the circulation may produce enlargement in such conditions as cirrhosis of the liver thrombosis of splenic or portal vein Banti s syndrome congestive heart failure or a movable spleen It is said that *in aortic regurgitation the enlarged organ* may pulsate Even secondary neoplasms may produce a palpable spleen and amyloid infiltration must also be taken into account Of the primary blood diseases

# Chapter 26

# Diseases of the Spleen and the Reticulo-endothelial System

By EDWARD B KRUMBHAAR M D and R PHILIP CUSTER M D

As the spleen is an important member of the reticulo-endothelial system and shares most of its lesions with the other members it is appropriate to consider their diseases together

## THE SPLEEN

THE peculiar anatomy and complex physiology of the spleen make it unusually important for the clinician to be conversant with its peculiar histologic structure, its unique circulatory arrangement * and its capacity as a blood cell reservoir which is second only to that of the liver (Barcroft *et al* ) It is also an important site for the elimination of blood cells apparently acting both as a graveyard and a slaughter house In the leukemias, it contains great numbers of the offending white blood cells (whether by infiltration or local proliferation or both) It appears to have indirect influences on the bone marrow and peripheral blood—peripheral erythrocytes being temporarily fewer in number but more resistant to hemolytic agents after removal of the normal spleen and platelets more numerous whether previously present in normal or decreased numbers The temporary marked increase of neutrophils after splenectomy may be later followed by temporary lymphocytosis and lymph node enlargement There is evidence still inconclusive, of splenic association with endocrine organs and relationships to anti body formation and tumor resistance The spleen is not essential to life in fact, after splenectomy most (or all) of its functions are gradually taken over by other organs

More frequently than any other organ of the body the spleen is found postmortem to be altered by disease in 10 000 autopsies at the Philadelphia General Hospital it was sufficiently changed to appear in the anatomic diagnosis in over 95 per cent In most cases, however the involvement was secondary and often unimportant For various conditions in which the spleen is importantly concerned such as the leukemias Hodgkin s disease polycythemia pernicious anemia the two forms of spherocytic jaundice and Banti s syndrome, the reader is referred to other portions of this book

### DIAGNOSIS OF SPLENOMEGALY

As most disorders of the spleen are accompanied by an enlargement † usually palpable or even extending to the brim of the pelvis the diagnosis of the kind of spleno-

* Fluctuating opinions on the open versus the closed intermediary circulation having veered toward the closed theory after Knisely s studies now lean more toward the open system (A O Whipple) This is important in the pathogenesis of many splenic disorders cp the engorged pulp and relatively empty sinuses of chronic hemolytic jaundice

† Examples weighing up to 8 kilos have been reported whereas Boscus spleen weighing 30 lbs (Lieutaud Historia Anatomico Medica 1767 I p 217) lacks conviction

creasing fibrosis produces a smooth hard rounded spleen cyanotic induration, that should not present difficulties of diagnosis

## Abscess

Abscess is rare, usually hematogenous or the result of a septic infarct or extending from neighboring suppuration The *symptoms* are usually masked by the primary disorder unless a perisplenitis or a rupture with general peritonitis occurs Local pain and tenderness perhaps with a friction rub then accompany the usual signs and symptoms of a severe suppuration One can hardly expect to elicit fluctuation The abscess may rupture into the pleura peritoneum colon or stomach The *prognosis* is grave

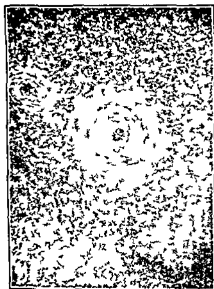


Fig 193 —Section of spleen in Feitis Fleckmilz showing an arteriole with proliferation of the wall especially the intima and a smaller one with hyaline change and beginning fibrosis of pulp (U of Pa Aut 42-17) × 54

*Treatment* —When diagnosed laparotomy is of course indicated As the diagnosis is rarely established before adhesions to neighboring structures have occurred or secondary abscesses formed splenotomy may be safer than splenectomy

## Infarction and Necrosis

Splenic infarction the result of endocarditis septicemia or atheroma of the aorta usually occurs without being recognized clinically If the embolus is sterile the simple anemic infarct is eventually replaced by scar tissue Occasionally a fresh hemorrhagic infarct may be found postmortem The rarer infected embolus causes a septic infarct which like the abscess is largely masked by the parent condition The abscess may be so large that the whole spleen is little more than a sack containing pus The *symptoms* of simple infarct are usually left upper quadrant pain exaggerated by respiration and tenderness Symptoms of septic infarct are like those of abscess The *treatment* is that of the underlying condition



Fig 194 —An almost completely obliterated arteriole surrounded by loose fibrous tissue and showing necrotic material above (U of Pa Aut 42-17) × 30

except for surgical relief of suppuration when present

The peculiar multiple necroses of Feitis (Fleckmilz) due to an obliterating arteriolitis are in themselves of no clinical importance but of considerable interest in relation to similar vascular lesions in the kidney and pancreas

pernicious anemia, the leukemias, hemolytic anemias, early sickle cell anemia and polycythemia all give moderate to extreme enlargement Exophthalmic goiter may be accompanied by enlargement at times considerable Of the primary diseases of the reticulo-endothelial system Gaucher's, Niemann Pick's and Hand Christian's syndromes and neoplasms are considered later in this chapter Banti's syndrome and hemolytic anemia (spherocytosis) are considered under Diseases of the Blood

## Anomalies

The spleen has been found either completely absent usually associated with other anomalies, or double (one of the two being ectopic) Accessory spleens are often found (31 4 per cent in Dorn's 1946 series) These share the fortunes of the larger organ, and therefore should usually be removed when splenectomy is being performed Anomalies of size and shape are of slight clinical importance

## Atrophy

As an organ rich in lymphoid material the spleen may become atrophic with increasing age (to 70 grams or less), though we *have found that it loses but little weight up* to the sixty-fifth year (normal average weight after removal 150 gms though probably much more in the living body) Atrophy occurs early in undernutrition, as in war edema and after experimental removal of the external function of the pancreas and is also found secondary to chronic congestion advanced arteriosclerosis or to local pressure In long standing sickle cell anemia marked fibrosis and atrophy (even less than 10 gms ) have been reported It is normally smaller in negroes than in whites and in women than in men per kilo of body weight

## Movable Spleen (Floating Spleen)

Movable spleens have been found in every part of the abdomen and in the pleural cavity in cases of diaphragmatic hernia *Symptoms* may be absent or part of a complex *of a general* visceroptosis Sometimes they are referred chiefly to some other organ disturbed by the spleen's malposition especially if adhesions have occurred The characteristic splenic notches are useful in *diagnosis*, together with the absence of normal dulness and occasional ability to return the organ to its normal bed

*Treatment*, desirable on general grounds and to forestall torsion, is the same as for general visceroptosis if mechanical supports prove useless splenectomy is indicated

*Torsion* — Torsion a not infrequent complication of movable spleen causes acute abdominal symptoms demanding immediate laparotomy Sudden pain shock enlargement of the spleen and often fever and vomiting are characteristic

*Rupture* —Traumatic rupture may occur in any enlarged diseased spleen or even in normal spleens 'Spontaneous rupture is rare being most often found in chronic malaria also in *infectious mononucleosis, leu*kemia Banti's syndrome torsion abscess infarct It has been reported even in apparently normal spleens Rupture into the peritoneum is often preceded for hours or *days by subcapsular hematoma Symptoms* are those of internal hemorrhage with local pain, abdominal spasm and limitation of left sided breathing They may not appear for some days after the trauma Surgical treatment is imperative and usually requires splenectomy The underlying mechanism is the increased intra abdominal or intrasplenic tension caused by the congestion edema and cellular hyperplasia which also obstructs blood vessels and thus promotes degeneration of the parenchyma and capsule

## Congestion and Acute Splenic Tumor

The acute splenic tumor of *infectious* diseases and intoxications is the commonest lesion of this organ being a combination of active hyperemia with a hyperplasia of both lymphoid and reticulo endothelial elements Found in most acute infections it may reach sufficient size to cause diagnostic difficulties The passive congestion of chronic heart disease or of any condition raising portal venous pressure (congestive splenomegaly) is also a frequent occurrence The pressure in the portal vein may rise to 250 or even 400 mm (water) In the course of time in

problem in management of the case. This primary type (i.e. with minimal tuberculous lesions elsewhere) according to Winternitz may attack either sex at any age (usually twenty to forty years). In the majority the painful somewhat tender enlarged organ was found associated with chronic digestive and respiratory disturbances weakness fever and emaciation. An unexplained tendency to polycythemia has been described. *Splenectomy* has proved a satisfactory form of treatment for these primary types.

*Malaria of the Spleen.*—The huge stone-like spleen of chronic malaria (ague-cake) was for centuries the most important form of splenomegaly until malaria came under the better control of specific treatment in recent times. The tremendous fibrosis often calcified and masses of pigment are characteristic *pathologic* features. The *symptoms* are those common to splenomegaly perhaps with the specific signs of malaria in the blood which should be sufficient for *diagnosis*. These large spleens are prone to rupture.

*Treatment.*—Splenectomy for those cases that do not respond to quinine or other antimalarial drugs must be considered. However it should be approached with greater caution than where elsewhere recommended on account of the numerous and complex adhesions which greatly increase the difficulty of removal. The survivors of this operation are usually greatly improved.

*Siderotic Splenomegaly (Gandi Gamna).* This condition may be mentioned here although the marked fibrosis with iron and calcium deposits has a varied etiology and similar lesions may be found in other organs.

## Cysts

Cysts of the spleen may be *simple* (traumatic embryonal defects dilated lymph spaces breaking down of hematomata and infarcts) *parasitic* (echinococcus) and *neoplastic* (dermoid angioma). If large enough to attract notice a fluctuating mass may be palpable and perhaps tenderness discomfort and a dragging sensation be produced. A quiet lesion may be activated by trauma. *Diagnosis* may be made by tapping though there is a slight danger of spreading a parasite or better by roentgen ray if the wall is sufficiently calcified or by splenectomy.

*Treatment.*—Partial resection is seldom indicated. In the non-parasitic forms, various mechanical supports may suffice. Splenectomy, if required is usually accomplished without difficulty.

## Neoplasms

Primary forms (malignant lymphoma and other types of sarcoma) are uncommon. Secondary tumors are probably not so rare as is usually thought arriving both by extension and by metastasis through blood and lymph channels. The primary site is commonest in the breast then in the skin (malignant melanoma) and next in the pancreas and the stomach. Benign tumors of the spleen are of no clinical importance. *Diagnosis* is usually too late to be of practical value although a few primary tumors have not recurred after removal. The traditional signs of pain and a growing mass in the left abdomen with increasing anemia and emaciation are suggestive when present.

## Hypersplenism

This term introduced by Eppinger (1913) to indicate an increased hemolytic activity of the spleen has come into wider use in recent years as a convenient explanation of the favorable effects of splenectomy in several conditions affecting erythrocytes granulocytes or platelets or all three. However Türk's aphorism (1914) still remains largely true: "The hemolytic diseases are the children and the spleen is their mother but the father is still unknown and possibly there are several fathers." How the spleen does harm other than by the direct action of its macrophages (seen in phagocytosis and in the smaller cell count in the splenic blood than in the arterial) still requires considerable elucidation. There is also at least suggestive evidence that pathological excess of a hormone-like substance manufactured in the spleen inhibits bone-marrow processes of blood-cell manufacture or maturation or both. If granulocytes are selectively in

### Amyloid Infiltration

(Waxy Degeneration, Lardaceous Diseases)

This lesion the spleen being the commonest site of amyloid disease, is most often associated with chronic tuberculosis next with chronic suppurative disease, slow malignant tumors, syphilis and cardiorenal disease in that order It may occur in the so called "primary" form where the "paramyloid" has a slightly different chemical structure The "sago spleen," i e, the follicular type causes little or no general enlargement and is of interest chiefly to the pathologist In one of our cases of primary amyloidosis, however, the markedly enlarged spleen ruptured spontaneously and was responsible for death of the patient In the diffuse form (bacony spleen) the palpable enlargement may be sufficient to cause discomfort (especially when lying on the right side) and possibly pain and tenderness For diagnosis the Congo Red test is useful, especially in secondary types The *prognosis* and *treatment* are those of the underlying condition, except when the great weight requires mechanical support or splenectomy Rarely the infiltration may regress, after removal of the primary cause

### Thrombosis of the Splenic Vein

Thrombosis of the splenic vein, either partial or complete, may produce symptoms lasting for years and distinguishable with difficulty or not at all from Banti s syndrome or other forms of chronic splenomegaly

*Symptoms and Diagnosis* —In acute thrombosis sudden abdominal pain, shock and painful enlargement of the spleen perhaps with gastric hemorrhage are suggestive The addition of ascites indicates portal involvement, and diarrhea with or without blood suggests involvement of the mesenteric vein In the chronic variety the above symptoms in milder and recurrent form together with a tendency to jaundice anemia and leukopenia and a spleen palpable in spite of ascites, give a picture that presents obvious difficulties especially when the symptoms are less pronounced A tendency toward exacerbations may be of diagnostic help If identified, either before or during laparotomy, splenectomy should be performed, and a porto-caval shunt considered if the portal vein is involved

### Cirrhotic Splenomegaly

Often a prominent and early manifestation of portal cirrhosis, this condition must be differentiated from other splenomegalies chiefly by an accurate history, supported by the various liver function tests and needle biopsy of the liver The smooth, firm, congested spleen resembles that of congestive heart failure Treatment should primarily be directed against the diseased liver Splenectomy has in some cases been attended by an improvement, especially in patients with esophageal varices, when it is accompanied by porto-caval shunt

### *Chronic Infectious Splenomegalies*

Space permits consideration here of only three chief varieties further details to be found in other appropriate chapters

*Syphilis of the Spleen* —Syphilis of the spleen a very rare condition nowadays, may occur either in the congenital or acquired forms of the disease in the former case signs being manifested in the first few months of life It appears much more frequently as an enlargement due to diffuse fibrosis (spirochetes rare or absent) than as single or multiple gummata The *diagnosis* depends on the accompanying signs of syphilis, together with an otherwise unexplained palpable spleen and tendency to jaundice and ascites The possibility of the enlargement being due to syphilitic amyloid disease must of course, be considered

*Treatment* —If specific medical treatment fails splenectomy has at times not only produced rapid improvement but permitted the treatment of the general condition to become more efficacious than before

*Tuberculosis of the Spleen* —Tuberculosis of the spleen usually a minor involvement secondary to a more important focus elsewhere and manifested in miliary or conglomerate forms may on rare occasions assume a stellar role In this case the marked enlargement often a single large mass designated as a tuberculoma, may produce a palpable spleen which constitutes the chief

The effects of splenectomy can be partly deduced from the opening statements of this chapter More precise details can be found in recent textbooks of surgery and in Coller s monograph on Indications for and Results of Splenectomy

## THE RETICULO ENDOTHELIAL SYSTEM

Cells of the reticulo-endothelial system are distinguished by their remarkable phagocytic property Their avidity for particulate matter injected into the blood stream of experimental animals led Aschoff and others to regard the aggregate of such cells as a functional unit despite their widespread distribution throughout the various organs and tissues of the body Reticulum cells (fixed histiocytes fixed macrophages) are found in intimate relation with delicate argyrophilic fibrillæ of the tissue framework as well as in the adventitia of small vessels The endothelial elements (to be distinguished from adult vascular lining endothelium) lie along certain blood and lymph sinuses Reticulo-endothelial cells are most abundant in the bone marrow spleen and lymph nodes and include the Kupffer cells of the liver The fixed reticulum and endothelial cells may transform themselves into free ameboid forms (wandering histiocytes wandering macrophages) which may in turn resume a fixed tissue position

The system is capable of progressive hyperplasia sometimes to an extreme degree This feature has partly obscured the experimental results of so called blockade of the system with various colloidal substances because the blockage itself induces such rapid hyperplasia that unblocked cells are ever present in considerable numbers

Continued studies on cells of the reticulo endothelial system have indicated that phagocytosis is but one of their functions that they are probably counterparts of embryonal mesenchymal cells and that they apparently retain the differentiative qualities of mesenchymal cells throughout post natal life particularly as regards hematopoiesis They remain the stem cells of the blood both within the bone marrow and as sources of extramedullary hematopoiesis (myeloid metaplasia)

Under physiologic conditions the cells of this system are concerned with the disposal of effete erythrocytes through phagocytosis The breakdown of the hemoglobin molecule within these cells probably begins with separation of the protein, globin, from the iron-containing fraction hemochromogen Hemochromogen is oxidized to hematin which undergoes further resolution to bilirubin and hemosiderin Bilirubin is excreted by the liver most of the hemosiderin is re used in the synthesis of hemoglobin Worn out leukocytes and thrombocytes are likewise removed by the reticulo-endothelial cells although many leukocytes pass out of the body in the saliva and along mucous membranes especially the gastro-intestinal

The phagocytic function of the reticulo endothelial system is further concerned in maintenance of health by removal of the small numbers of bacteria and inert foreign substances that constantly enter the blood and lymphatic streams Organic foreign matter is digested by intracellular enzymes while inorganic material such as carbon is retained in more or less innocuous desuetude The role of the reticulo endothelial system in the production of antibodies has been challenged by recent studies which indicate that plasmocytes and lymphocytes are more directly concerned However it must be remembered that these two more specialized cell types are direct descendants of reticulo-endothelial elements

### Disorders of the Reticulo-Endothelial System

One may broadly classify disorders of the reticulo-endothelial system as (1) reactive hyperplasias and (2) neoplastic diseases The first group comprises most commonly the chronic granulomatous processes infectious or otherwise in which the response of histiocytes (macrophages) to the noxious agent is outstanding such as in histoplasmosis Boeck s sarcoid silicosis and so on More specifically linked with the reticulo endothelial system are the so called lipodystrophies where the reactive hyperplasia may assume widespread and massive pro

volved, primary splenic neutropenia (Wiseman and Doan, 1942) results if platelet formation is damaged by excessive "thrombocytopen" a lipid formed in the spleen (Moolten *et al*, 1949), thrombocytopenic purpura develops Inhibited formation or excessive destruction of red and white blood cells, and platelets may be caused by panhypersplenism or splenic panhematopenia' (Doan and Wright, 1946) These conditions as in the case of congenital and acquired familial hemolytic anemia, can occur in either primary or secondary forms Differentiation of primary from secondary cases is important as splenectomy is chiefly valuable in the primary forms In fact, it is contraindicated in secondary cases in which a removable cause is found or extramedullary hematopoiesis is compensatory and a more potent factor than the hypersplenism

For the diagnosis of hypersplenism, one expects to find an enlarged spleen (except in most cases of thrombocytopenic purpura) in the peripheral blood a decreased number of erythrocytes granulocytes or platelets, as the case may be a well functioning generally hyperplastic bone marrow (sternal puncture), and an over-active spleen sometimes demonstrated by the epinephrine test This test is done by Doan as follows

> During a fifteen to thirty minute base-line period, under basal metabolic conditions the pulse, blood pressure and two preliminary complete peripheral blood studies are obtained and the splenic outline is traced Depending upon the age and vascular integrity of the patient 0 5 to 1 cc of 1 1000 adrenalin chloride is injected subcutaneously Blood studies are repeated at ten minute intervals until the pulse and blood pressure reach their maximum stimulation which usually coincides with the greatest contraction of the spleen The peripheral blood studies are then continued at fifteen minute intervals until the spleen has relaxed and the biphasic depression of the curve has been obtained
>
> A positive result is indicated by a significant rise in the peripheral blood level of the affected cell type

## SPLENECTOMY

As an intact spleen is not essential to health and can be removed with relative ease unless bound down by adhesions this procedure naturally often comes into consideration In addition to its use in several surgical conditions splenectomy is accepted these days at least as definitely indicated in cases of hereditary spherocytic anemia idiopathic thrombocytopenic purpura, and the hematopenic conditions where ill health persists and no removable cause can be found It has been found valuable in selected cases of a considerably larger group Lahey and Norcross for instance (1948) had good results in the majority of their cases of congestive splenomegaly (especially if taken early) various secondary thrombocytopenic purpuras, idiopathic acquired hemolytic anemia (spherocytosis and fragility of red cells demonstrated in about half the cases) panhematopenia and cysts of the spleen Sustained improvement has sometimes been observed after removal of chronically enlarged spleens in cases of malaria syphilis sickle-cell anemia Gaucher s and even Hodgkin s disease and the leukemias Lahey indeed maintains that splenectomy is indicated whenever the enlargement has lasted for 6 months or more in a well studied case of obscure origin where there is no definite contra indication also that the indication in the individual case rests more with the hematologist than with the surgeon The mortality, which has attained 3 per cent in the best clinics in recent years, should not exceed 5 or 10 per cent Splenectomy is of course contra indicated for metastatic cancer acute leukemia pernicious anemia agnogenic myeloid metaplasia which we regard as a variant of chronic granulocytic leukemia and acute infections and certainly for most other cases of chronic leukemia Hodgkin s disease chronic infections and depressions of hemopoiesis due to removable causes In myeloid metaplasia where the splenic changes are mainly compensating for an incompetent bone marrow splenectomy not only is harmful, but may rapidly cause death

In Felty s syndrome where the splenomegaly has often been found to be due to amyloidosis splenectomy is not indicated nor is the arthritis improved by the operation

Irradiation of the splenic area and ligation of the splenic vein rarely produce some of the effects of splenectomy although both have been advocated in selected cases but without extensive adoption

*Prognosis*.—If the disease becomes manifest in infancy or the central nervous system is involved the outlook is not favorable. The average duration, however, is about 20 years and many patients survive much longer. So-called carriers may never show evidence of the disease.

*Treatment*.—Splenectomy is the only procedure that has proved of value. Transfusions of whole blood before during and after operation lessen the risk materially. The thrombocyte count should be followed carefully after operation and should the level rise well above normal the use of anticoagulant therapy needs be seriously considered. Because the disease is a generalized one, splenectomy cannot be regarded as a cure.

### Niemann-Pick's Disease

This rare disorder occurs in infancy, most cases having been found in Jewish females with no familial tendency evident. It is characterized by extensive accumulation of lipids throughout the reticulo-endothelial system.

*Pathology*.—Virtually all organs are involved and enlarged, more particularly the spleen and, to lesser degree, the liver and lymph nodes. The bone marrow is more or less extensively displaced and the bone cortex thinned. Tissue changes resemble those of Gaucher's disease except that the lipid histiocytosis is more widespread. The characteristic cell is from 20 to 80 microns in diameter and the cytoplasmic vacuoles are spherical. The lipid filling the vacuoles is chiefly a phosphatid (sphingomyelin) which accepts Sudan dyes and Nile-blue sulfate and is soluble in the usual fat solvents. Hemosiderin is not demonstrable in the cells. Lipid deposits have also been noted in ganglion and glial cells.

*Symptoms*.—Gastro-intestinal disturbances usually the first signs of the disease may be found within the first few weeks or months of life. Poor nutrition, retarded development and edema supervene often associated with a brownish pigmentation of the skin. A cherry-red spot in the retina near the macula, typical of amaurotic family idiocy, is sometimes observed. A protuberant abdomen calls attention to the enlarged spleen and liver, and superficial lymph nodes are often prominent. Radiologic studies may demonstrate osteoporosis.

Anemia is not usually severe although hypochromia is sometimes marked owing to general malnutrition and iron deficiency. Neutropenia and relative or absolute lymphocytosis (up to 40 000) and monocytosis are frequently noted. The large lipid bearing histiocytes occasionally enter the circulating blood.

*Diagnosis*.—Differentiation from the infantile form of Gaucher's disease may sometimes prove difficult on clinical grounds alone. Aspiration of the bone marrow or spleen or biopsy of a lymph node will establish the diagnosis conclusively on the basis of cytoplasmic differences already described.

*Prognosis*.—The outlook is bad, the course of the disease being relatively acute. Patients seldom survive the third year of life with death usually resulting from intercurrent infection.

*Treatment*.—Splenectomy has effected temporary improvement in some cases, none in others. Blood transfusions and antibiotic therapy may be employed as indicated to combat infection.

### Hand-Schuller-Christian's Disease

The picture of exophthalmos, diabetes insipidus and yellowish softened areas in the cranium was first mentioned by A. Hand in 1893 but not generally recognized until after Christian's report in 1919 since which time a surprising number of cases have been described in this category. The cause still remains obscure.

The syndrome is manifested chiefly in childhood and somewhat more in males than females, but no racial or familial predisposition has been demonstrated.

*Pathology*.—As in the previous two diseases excessive lipids are found in the cells of the reticulo-endothelial system. Chemical analysis of the tissues shows a high content of cholesterol, cholesterol esters, neutral fat and lecithin. As the disease progresses fibroblastic proliferation becomes more evident and there is an associated eosinophilic

portions, being concerned with the intracellular storage of atypical or over abundant lipids (Gaucher's, Niemann-Pick's Hand-Schuller Christian's diseases xanthomatosis, diabetic lipemia, cholesterolosis), and these are the ones to be considered in this chapter Eosinophilic granuloma of bone, because of its probable relationship to Hand-Schuller-Christian's disease will also be included Letterer-Siwe's disease (nonlipid histiocytosis) is mentioned in this chapter, although its truly neoplastic nature is not yet well established

Neoplasms of the reticulo-endothelial system encompass the malignant lymphomas including Hodgkin's disease, the various leukemias (leukemic and aleukemic) erythremia (polycythemia rubra vera), and myelomatosis These conditions are discussed elsewhere in the book

## Gaucher's Disease

This is an uncommon disease of obscure nature and is transmitted as a Mendelian dominant character the carriers frequently being unrecognized except on biopsy It chiefly afflicts Jewish women It is probably a metabolic disorder concerned with the deposition of complex lipoproteins

*Pathology* —When the disease is well developed, the spleen is generally huge (3 to 4 kilos), firm, and smooth, with pale red exterior, and a granular cut surface with yellow or grayish red irregular spots divided by darker red bands The liver is also enlarged presenting a relatively firm pallid parenchyma Lymph nodes may also be involved In advanced cases bones may be rarefied to a marked degree

The tissues in general but notably the spleen, liver lymph nodes and bone marrow contain nests of so-called Gaucher cells usually in alveolar arrangement sometimes in diffuse sheets The Gaucher cells vary from 20 to 80 microns in diameter and have one or several small eccentrically placed nuclei The bulky cytoplasm is faintly acidophilic, and is only lightly stained by Romanowsky techniques A fibrillar cytoplasmic network can be demonstrated by Mallory's aniline blue-orange G method the characteristic lipid (kerasin a cerebroside or cerebroglycoside) being deposited between the meshes The usual fat solvents will not dissolve kerasin, and it is, at most only faintly stained with Sudan III The cells also contain a few granules of hemosiderin, demonstrable by the Prussian blue reaction

*Symptoms* —The disease usually becomes manifest in early life, occasionally later and pursues a very chronic course Symptoms are generally related to the large spleen which produces discomfort in the left side of the abdomen, sometimes with pain radiating down the left leg The liver and lymph nodes are often palpably enlarged The skin is frequently discolored from a yellow to gray-brown, and wedge shaped pingueculæ of the conjunctiva are not uncommon in adults Indirect illumination may be required to demonstrate the conjunctival lesions Roentgenologic study discloses rarefying bone lesions in most cases and pathological fractures have occurred The central nervous system has occasionally been involved the manifestations of which naturally depend on location of the lesion

Blood studies in some cases show a slight to moderate degree of anemia which is normocytic in type without much evidence of regenerative activity of the marrow Generally, one finds an associated neutropenia and slight decrease in thrombocytes Gaucher cells are rarely encountered in blood smears When the skeleton is widely involved marrow displacement may be so extensive that the anemia leukopenia and thrombocytopenia are very marked In other patients the anemia or panhematocytopenia is apparently due to hypersplenism as evidenced by striking remission after splenectomy

*Diagnosis* —A positive family history chronic marked splenomegaly starting in a young person moderate anemia leukopenia and perhaps thrombocytopenia conjunctival thickening skin pigmentation, and possibly lesions of the bony structure or central nervous system should suggest Gaucher's disease Positive diagnosis rests with the demonstration of the typical cells which may be obtained in virtually all cases by aspiration of the bone marrow Splenic puncture has also been employed in diagnosis Chemical analysis of tissue is confirmatory but not necessary

and plasmocytic reaction and lipid laden histiocytes may be sparse

While the destructive lesions of membranous bones (especially skull pelvic girdle vertebræ) are the most striking any tissue may be affected and biopsy of the bone marrow may show the lipophagic granulomatosis in area not associated with bone rarefaction

*Symptoms*—The insidious onset with underdevelopment (sometimes amounting to actual dwarfism) headaches drowsiness and bone pains is usually manifested in the second or third year The classical syndrome of defects in membranous bones exophthalmos (usually unilateral) and diabetes insipidus is based merely on the fact that in about 85 per cent of cases the bones around the sella turcica and orbit are involved to a major degree with consequent damage to the pituitary and hypothalamus and extension of the granulomatous tissue into the retrobulbar space Deafness and otorrhea result from deposits in the temporal bone while tender gums and loose carious teeth follow involvement of the alveolar processes

Nonregenerative anemia leukopenia and thrombocytopenia of mild-to-moderate degree are sometimes seen and are occasionally marked when marrow displacement is advanced Hypercholesterolemia is commonly found

*Diagnosis*—The symptom complex already mentioned makes the diagnosis easy in the majority of cases Biopsy of an accessible lesion is helpful When older persons are affected the diagnosis may be much more difficult and made possible only by biopsy Though eosinophilic granuloma of bone is regarded as closely allied to Hand Schuller Christian s disease it is important to make the distinction because eosinophilic granuloma is usually responsive to roentgen therapy, whereas typical Hand Schuller Christian s disease is seldom if ever benefited

*Prognosis*—When the disease begins in early childhood the life expectency is seldom more than from 1 to 4 years The outlook is distinctly better in the older age group

*Treatment*—No specific treatment has been evolved Dietary regulation seems rational especially restriction of fats A trial of roentgen therapy is worth while especially if there is any question of eosinophilic granuloma in the differential diagnosis *

* Without actual figures in support we are of the opinion that of the three diseases just mentioned *Gaucher s disease is the commonest* Hand Schuller Christian s next commonest and Niemann Pick s rarest

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LEGEND FOR FIGURE 195

FIG 195 —*A Gaucher s Disease* —Reticulo-endothelial cells of the bone marrow richly laden with kerasin displacing the fat and hematopoietic tissue normal to this location Cells of the reticulo-endothelial system elsewhere notably in the spleen show the same changes (H and E stain × 900)

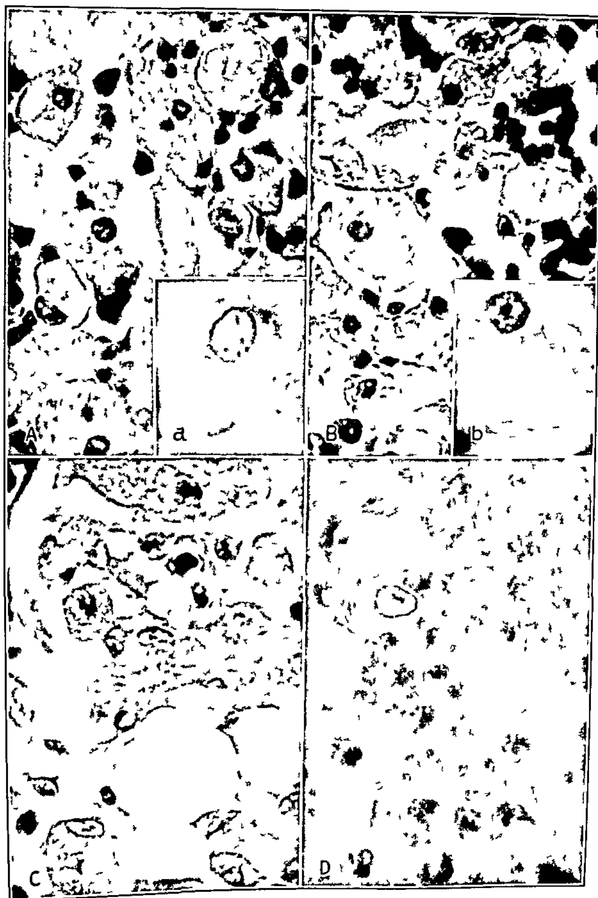
*a* Higher magnification of a Gaucher cell showing the reticulated appearance of the cytoplasm (Mallory s aniline blue- orange G stain × 1890)

*B Niemann Pick s Disease* —Reticulo-endothelial cells of the bone marrow distended with sphingomyelin As in Gaucher s disease this abnormal storage takes place throughout the reticulo-endothelial system (H and E stain × 900)

*b Higher magnification shows the cytoplasm to contain the lipid in both large and fine spherical vacuoles* in contrast to the veining noted in the Gaucher cells (Mallory s aniline blue orange G stain × 1890)

*C Hand-Schuller Christian s Disease* —Section through a defect in a membranous bone discloses an abundance of foam cells the lipid content of which is mainly cholesterol cholesterol esters neutral fat and lecithin (H and E stain × 900)

*D Eosinophilic Granuloma of Bone* —Section through an osteolytic lesion of the tibia presents an abundance of eosinophils readily distinguished by their coarse granularity distributed amongst a background of reticulum cells which have large vesicular nuclei (H and E stain × 1350)




Legend for Figure 195 at Bottom of Page 1225

COLLER F A BLANE A and GOULD A Indications for the Results of Splenectomy Springfield Ill Charles C Thomas 1950

CUSTER R P An Atlas of the Blood and Bone Marrow Philadelphia, W B Saunders 1949

DOAN C A Differential Diagnosis and Treatment of Diseases Involving the Spleen West Va Med J 1945 *41*, 121

DOAN C A and WRIGHT C S Primary Congenital and Secondary Acquired Splenic Panhematopenia Blood 1946 *1* 10

EPPINGER H Die hepatolienalen Erkrankungen Berlin Julius Springer 1920

FOWLER R H Cystic Tumors of the Spleen Surg Gyn and Obst 1940 *60* 213

GROEN J The Hereditary Mechanism of Gaucher s Disease Blood 1948 *3* 1238

HAND A Proc Phila Path Soc 1891–1893 *16* 282

KNISELY M N Spleen Studies Anat Rec 1936 *65* 23 and 131

KRACKE R R and RISER W H JR The Problem of Hypersplenism J Am Med Assn 1949 *141* 1132

KRUMBHAAR E B Functions of Spleen Physiol Rev 1926 *6* 160

LAHEY F H and NORCROSS J W Splenectomy When is it Indicated Ann Surg 1948 *128* 363

MOOLTEN S E *et al* Rôle of Blood Platelets in Thromboembolism Arch Int Med 1949 *84* 667

NIEMANN A Ein unbekanntes Krankheitsbild Jahrb f Kinderh 1914 *79* 1

PEARCE R M KRUMBHAAR E B and FRAZIER C H The Spleen and Anemia Philadelphia J B Lippincott Company 1917

SOHELLING D H and VOSHELL A F Xanthonatosis generalisata ossium Arch Int Med 1935 *55* 592

WHIPPLE A O Problem of Portal Hypertension in Relation to the Hepatosplenopathies Ann Surg 1945 *122* 449

WISEMAN B K and DOAN C A Primary neutropenia Am Int Med 1942 *16* 1097

WOHL MICHAEL G Spontaneous Rupture of the Spleen Ann Surg August 1925

WRIGHT L T and PRIGOT A Traumatic Subcutaneous Rupture of Normal Spleen Arch Surg 1939 *39* 551

### Eosinophilic Granuloma of Bone

These destructive granulomas of bone may be single or multiple and have been found in all bones except those of the hands and feet, the predilection being for the skull vertebrae, ribs, pelvis, humerus, and femur The lesions have occurred mainly in children and young adults, especially males Tenderness and swelling over the bone generally serve to call attention to them, and roentgenograms show irregular areas of radiolucency These must be differentiated from primary or secondary neoplasms

Tissue curetted from the bone defects is yellowish brown and friable, often with areas of hemorrhage The histologic appearances vary from broad sheets of macrophages, suggestive of tumor at first glance to areas in which admixtures of lymphocytes, plasmocytes, fibroblasts, neutrophils and especially eosinophils signify an inflammatory process Multinucleated giant cells are characteristically found Necrosis and hemorrhage may be extensive As the lesions progress the macrophages engulf fatty substances from the displaced marrow and large foamy cells may predominate simulating the lesion of Hand-Schuller Christian's disease very closely Finally, fibroblastic proliferation may result in spontaneous regression of the lesion and the residual scar may resemble fibrous dysplasia of bone Laboratory studies, apart from showing occasional mild eosinophilia, are not helpful in establishing the diagnosis and microscopic examination of curettings from an affected bone is essential

Healing generally follows curettage of the lesion Equally good results often are obtained by roentgen therapy

### Letterer-Siwe's Disease

This disease is regarded by some authors as another expression of the basic disorder underlying eosinophilic granuloma and Hand-Schuller Christian's disease There is the same focal and diffuse proliferation of histiocytes throughout the tissues, but without the presence of demonstrable lipids within the cells

The disease is characterized clinically by fever, skin rash, progressive hypochromic anemia, and purpura, occasionally with focal destruction of bone It occurs mostly in infants and runs a rapid and inevitably fatal course Whether this disease is inflammatory metabolic or neoplastic still remains a question

### Xanthomatoses and Hypercholesteroloses

A group of clinical syndromes, all associated with orange or yellowish lipid deposits in cells of the reticulo endothelial system mostly in the skin, is included under this heading Recognized varieties are xanthelasma (yellow ovoid papules of the eyelids), juvenile xanthomas of the skin (which tend to be familial), xanthoma tuberosum multiplex (which frequently involve tendon sheaths as well as skin), xanthoma disseminatum (which may affect both skin and mucosa of pharynx and larynx), xanthoma diabeticorum (associated with diabetic lipemia) xanthomatosis generalisata ossium (Shelling and Voshell, 1935), and so-called generalized visceral xanthomatosis

In the early stages of these conditions histologic examination discloses poorly defined nests of lipid laden histiocytes comprising the local lesions There may be an associated inflammatory reaction in the periphery and proliferating fibroblasts not infrequently mask the basic picture The lipid is soluble in the usual fat solvents and shows affinity for fat stains

Hypercholesterolemia is common to this group of conditions, and restriction of fat in the diet is the logical approach to the more widespread or troublesome forms The use of lipotropic substances (choline methionine inositol) may possibly help Xanthoma diabeticorum is generally relieved by adequate treatment of the underlying condition Most of the lesser lesions require no therapy

### References

Aschoff L Lectures in Pathology New York Paul B Hoeber Inc 1924

Barcroft J Spleen Lancet 1925 *1* 319

Christian H A Contributions to Medical and Biological Research New York Paul B Hoeber Inc 1919 *1* 390

will, to an extent, vary with individual pain thresholds and with the descriptive terms used. "Heartburn," "gnawing pain," "boring pain," "cramplike pain," "distention," and "gas," for example, may all represent similar underlying processes; the variety is in the degree and the descriptive terms. A burning sensation in the epigastrium or under the sternum—the sensation usually described as heartburn—may be experimentally produced by local balloon distention in the lower esophagus or duodenum. It seems to be essentially motor in character rather than dependent upon chemical changes affecting the mucosa. It is obvious, however, that local ulcerative breaks in the integrity of the mucosa may result in chemical stimulation of the sensory nerves exposed to irritating secretions and therefore also produce a sensation of pain.

It is important to recognize that, as a rule, symptoms arising from the alimentary canal are typically referred to certain segmental areas of the body, a fact of great diagnostic significance in the interpretation of individual histories. Thus disturbances of the upper esophagus are usually productive of symptoms perceived anteriorly under the upper third of the sternum; from the midesophagus under the midsternum; and from the cardiac end of the stomach under the lower third of the sternum or the xiphoid. Gastric disease productive of symptoms usually causes pain referred to the midepigastrium, as does disease in the first portion of the duodenum. In the second and third *portions of the duodenum, sen*sation is usually referred to the midline or somewhat to the right halfway between the xiphoid and the umbilicus. Disease of the jejunum and ileum usually causes discomfort or pain in the periumbilical area, whereas lesions at the ileocecal junction or in the appendix are likely to cause pain at a point halfway between the right anterior superior spine of the ilium and the umbilicus (McBurney's point). Disease of the colon, for the most part, produces hypogastric pain at a level below a line going from one anterior iliac spine to the other. Diseases arising at or near the hepatic or splenic flexures are usually perceived at the point of stimulation or close to it. Sigmoidal pain is most frequently experienced in the left lower quadrant approximately over the course of the sigmoid. Symptoms arising from the rectosigmoid and rectum are usually felt just above the symphysis pubis or in the perineum. It should be pointed out that at any level symptoms may also be felt in the midline of the back at the same segmental level as that of the anterior pain; in some instances only the back pain may occur. If the pain is intense, it may spread laterally from the anterior or posterior points of reference and surround the segment in a zonal distribution. It is obvious that such general localization of pain is subject to variation, and bizarre distributions may be encountered from time to time in individual patients. The presence of major operative scars either in the thorax or in the abdomen frequently causes a deviation of pain reference from the customary site of reference to the scar. Furthermore, lesions involving the general area just above and below the cardiac sphincter are associated with pain almost indistinguishable in distribution from that of angina pectoris, the pain radiating to the shoulder, the arm, and the fingers. The mechanism of pain production by disease of the biliary tract or pancreas probably involves two separate factors. Stretching of the liver capsule or the pancreas secondary to underlying disease may cause steady dull pain, a pain usually referred to a spot over the organ involved. When that organ is the pancreas, back pain at or near the level of the pancreas *and usually somewhat to the left of the spine* is fairly common. If a calculus or some other mechanical block partially obstructs the flow of bile or pancreatic juice, the resulting pain is undoubtedly due to increased tension of the smooth muscle of the duct just above the point of obstruction or of the entire ductal system. Peritoneal irritation due to focal inflammatory disease or metastatic involvement is associated with pain and tenderness over the exact area involved.

The diagnosis of alimentary tract disease must be based on a careful case history, a thorough physical examination, skillful roentgen ray studies, the selective use of appropriate endoscopic procedures, and well chosen laboratory measures. Mistakes in

# Chapter 27

# Diseases of the Alimentary Tract

By CHESTER M JONES MD

*General Considerations of Digestive Tract Disease* —The multiplicity of factors capable of causing digestive symptoms is due to the highly complicated nerve supply of the entire digestive tract the interplay of hormones on the various elements of the tract, and its exposure to numerous irritating or noxious agents For this reason, the successful diagnosis and treatment of digestive diseases must be based on a general understanding of fundamental physiological principles as well as on a knowledge of anatomical details and morphological changes secondary to specific disease processes Unless it is backed by a very sound knowledge of all the facets of internal medicine, gastroenterology indeed becomes too limited a specialty Furthermore a successful approach to the problems of alimentary tract disease must imply the closest collaboration between well trained internists and equally well trained surgeons Because the general nutrition of the body depends in large part upon the normal functioning of the alimentary canal a further comprehension of the principles of dietary adequacy is essential Finally because the entire functioning of all the organs of digestion (in the presence or absence of morbid changes) may be seriously modified by emotional difficulties an awareness of present-day psychiatric practice and thinking is highly necessary

Symptoms arising from the alimentary canal are essentially due to neuromuscular disturbances at one level or another These may be secondary to local or general inflammatory changes local changes in blood supply or alterations in the secretory processes at one level of the tract or another, with resulting changes in digestive and absorptive processes Hypermotility over a small or large segment of the tract, for example may be produced by a specific inflammatory process a new growth or an anatomical abnormality a partially occluding foreign body within the lumen of the tract or occlusion of a localized vascular area supplying the affected portion of the tract with blood Similarly, it may be caused by increased stimulation of the autonomic nervous system Diminished or absent motility with subsequent distention and resulting symptoms may be due to such factors as the administration of narcotics damage to the spinal cord wasting disease with atrophy of the musculature of the intestinal tract and lack of intestinal tone (as in hypokalemia or uremia) or to the distention secondary to the inadequate or delayed carbohydrate digestion and absorption encountered in pancreatic disease the sprue syndrome and the like In any event symptoms arising from the alimentary canal are primarily associated with abnormal smooth muscle function leading to focal or more generalized increase in propulsive activity local spasm or local distention Thus abdominal pain may be produced by the spasm secondary to the administration of morphine or lead to focal ulceration or inflammation or to a more generalized inflammatory process with hypermotility The kind and the degree of the symptoms

as pneumonia typhoid *etc* In the more chronic form of malnutrition the maroon coloration of the tongue is commonly associated with lack of riboflavin or pyridoxin in the diet In pellagra, the tongue is typically red extremely sensitive and atrophy may be more or less a striking feature This appearance may be due in part to nicotinic-acid deficiency, but it is quite probable that other factors are also involved A somewhat different manifestation of a specific dietary deficiency is that encountered in scurvy in which there is a striking swelling of the gums which are not only hyperemic but very spongy and which bleed readily They may become so painful that eating is difficult and loosening of the teeth may occur These manifestations are specifically due to a lack of vitamin C in the diet In pernicious anemia a smooth red, and intensely sore tongue may also be noted but it is not a necessary manifestation of the disease A similar appearance is to be noted in sprue of rather severe grade or of long standing Complete atrophy of the papillae of the tongue, with or without accompanying soreness and superficial ulceration and usually with extreme pallor is encountered in the so-called Plummer-Vinson syndrome and is probably due to iron deficiency as the major contributing factor although there are undoubtedly other nutritional deficits In a given case the degree of papillary atrophy of the tongue or the intensity of the redness may provide a proper measure of the severity of the malnutrition, which may be due solely to dietary inadequacy to specific factors (as in pernicious anemia) or to underlying alimentary tract disease (which may be the cause of anorexia nausea vomiting or diarrhea) Cheilosis may accompany any of these manifestations of deficiency disease Corrective therapy may be limited simply to the provision of specific substances such as riboflavin nicotinic acid and vitamin $B_{12}$ or may merely involve the administration of a general diet that is well balanced and adequate If the changes are secondary to underlying digestive tract disease improvement cannot be satisfactorily achieved until the fundamental process has been sucsessfully attacked

*Infectious Diseases* —The buccal manifestations of infectious disease must include a consideration of such specific infections as measles scarlet fever smallpox, chickenpox syphilis tuberculosis leprosy, and histoplasmosis The Koplik's spots of measles and the strawberry tongue of scarlet fever are usually characteristic and easily recognized The eruption of smallpox and the vesicles of chickenpox regularly appear upon the tongue the palate and the inner surfaces of the cheeks Syphilis, in all its stages may involve changes in the mucous membrane of the mouth These may appear as a chancre of the lip or tongue or as mucous patches on the tongue the lips and the buccal surfaces Condylomata may be seen in the angles of the mouth and, late in the disease gummatous lesions may involve the tongue the lip or the hard palate The diagnosis may be made by dark field examination of material obtained from the lesions or by observation of the associated stigmata of syphilis in other parts of the body Tubercular lesions are most common on the lip the edges of the tongue and the soft palate They are characterized by primary yellowish nodules which gradually ulcerate and enlarge Tubercle bacilli can usually be demonstrated in the discharge from the ulcers Histoplasmosis may cause ulceration of the tongue the lip or the pharynx There is usually involvement of adjacent nodes Diagnosis may be made by discovery of other evidence of the disease or by local biopsy In typhoid fever ulcerations of the mouth are not uncommon They are associated with other manifestations of the disease The lesions of herpes simplex activated by other infectious diseases such as pneumonia epidemic meningitis *etc* may be characterized by vesicle formation and subsequent ulceration the lesions appearing on the lips under the tongue or at the base of the alveolar processes Ulcerative stomatitis may occur in children or in adults and seems to be associated with general dietary deficiency and such local devitalizing factors as dental sepsis It is accompanied by swelling and hyperemia with subsequent necrosis and ulceration along the border of the gums and extension of that necrosis and ulceration to the cheek

diagnosis are more frequently due to an inadequate case history than to any other single cause, a careful and detailed history usually leads to a properly directed and successful search for disease at one level or another *Physical examination, although* of the utmost importance is secondary unless the disease to be diagnosed is so far advanced as to be easily recognized The information obtained by physical examination often merely reflects a general state of nutrition indicative of the degree and duration of disease involvement Routine roentgen-ray studies are often unhelpful because the roentgenologist has not been fully told what the malady suspected is or where it is most likely to be manifested The physician and the roentgenologist should consult each other thoroughly before the *x* ray studies are made

Esophagoscopy, gastroscopy, sigmoidoscopy, and peritoneoscopy necessarily apply to special conditions and require carefully trained physicians Laboratory studies may be classified under two headings specific and general Demonstrating the presence of hyperbilirubinemia, for example or discovering pancreatic enzymes missing from the duodenal juice indicates clearly the site of disease But finding occult blood or undigested food elements in the stools indicates only the presence of an abnormality somewhere in the digestive canal and demonstrating the presence of anemia or hypoprothrombinemia though pointing to various sources for such abnormalities may indicate no more than the severity of some underlying disease Successful treatment obviously demands a demonstration of the specific disease process sought or absolute location of that process as well as a knowledge of the degree of physiological change the numerous factors involved may cause

Proper therapy of alimentary tract disease must include a real knowledge of the normal physiological factors controlling 'digestion," the typical pattern of symptoms associated with individual diseases or syndromes, and the specific measures—medicinal, dietary, and surgical—which may be used to restore or replace function or to remove the cause of focal symptoms The physician must also be fully aware of the dangers and risks associated with various therapeutic measures and the sequelae that may follow such procedures, particularly those related to properly standardized surgical maneuvers which, *nevertheless, may subsequently have a* profound effect upon the patient s nutrition and general health Many types of digestive-tract disease are chronic and are ultimately remediable by proper surgical procedures Physicians should not continue to employ relatively unsatisfactory medical measures when surgery will provide cure or at least reasonable protection against the major symptoms of a given malady A further warning may properly be stressed Many digestive diseases are marked by remissions and exacerbations which may occur spontaneously in the course of the disease rather than because of specific or general medical measures Temporarily excellent results may be erroneously attributed to specific programs or specific medications, these are then unduly prolonged at great expense to the patient but without any adequate therapeutic result In no field of internal medicine is it more important to develop a critical understanding of the life history of given diseases and the mode of action of various therapeutic principles

## DISEASES OF THE ORAL CAVITY

Disease conditions of the oral cavity may be divided into four classes (1) nutritional disturbances (2) specific infectious diseases (3) neoplasms and (4) local changes in the buccal mucosa or the gums changes secondary to specific therapeutic maneuvers noxious agents or constitutional disease

*Nutritional Disturbances* —The effects of malnutrition may frequently be noted in the buccal cavity insofar as these are reflected by atrophy of the papillae of the tongue *with or without local ulceration* along the edges or tip The atrophic process may be so extensive that the tongue is devoid of papillae and presents a totally smooth appearance Extreme redness and slight atrophy may be observed during the immediate postoperative period as a result of starvation and dehydration or it may occur in the course of an acute illness such

as pneumonia, typhoid, *etc* In the more chronic form of malnutrition the maroon coloration of the tongue is commonly associated with lack of riboflavin or pyridoxin in the diet In pellagra, the tongue is typically red, extremely sensitive, and atrophy may be more or less a striking feature This appearance may be due in part to nicotinic-acid deficiency but it is quite probable that other factors are also involved A somewhat different manifestation of a specific dietary deficiency is that encountered in scurvy in which there is a striking swelling of the gums which are not only hyperemic but very spongy and which bleed readily They may become so painful that eating is difficult and loosening of the teeth may occur These manifestations are specifically due to a lack of vitamin C in the diet In pernicious anemia a smooth red, and intensely sore tongue may also be noted, but it is not a necessary manifestation of the disease A similar appearance is to be noted in sprue of rather severe grade or of long standing Complete atrophy of the papillae of the tongue with or without accompanying soreness and superficial ulceration and usually with extreme pallor is encountered in the so-called Plummer Vinson syndrome and is probably due to iron deficiency as the major contributing factor although there are undoubtedly other nutritional deficits In a given case, the degree of papillary atrophy of the tongue or the intensity of the redness may provide a proper measure of the severity of the malnutrition, which may be due solely to dietary inadequacy to specific factors (as in pernicious anemia) or to underlying alimentary tract disease (which may be the cause of anorexia nausea vomiting or diarrhea) Cheilosis may accompany any of these manifestations of deficiency disease Corrective therapy may be limited simply to the provision of specific substances such as riboflavin nicotinic acid and vitamin $B_{12}$ or may merely involve the administration of a general diet that is well balanced and adequate If the changes are secondary to underlying digestive-tract disease improvement cannot be satisfactorily achieved until the fundamental process has been successfully attacked

*Infectious Diseases* —The buccal manifestations of infectious disease must include a consideration of such specific infections as measles, scarlet fever, smallpox, chickenpox syphilis tuberculosis leprosy, and histoplasmosis The Koplik s spots of measles and the strawberry tongue of scarlet fever are usually characteristic and easily recognized The eruption of smallpox and the vesicles of chickenpox regularly appear upon the tongue, the palate, and the inner surfaces of the cheeks Syphilis in all its stages may involve changes in the mucous membrane of the mouth These may appear as a chancre of the lip or tongue or as mucous patches on the tongue the lips and the buccal surfaces Condylomata may be seen in the angles of the mouth, and late in the disease, gummatous lesions may involve the tongue the lip or the hard palate The diagnosis may be made by dark field examination of material obtained from the lesions or by observation of the associated stigmata of syphilis in other parts of the body Tubercular lesions are most common on the lip the edges of the tongue and the soft palate They are characterized by primary yellowish nodules which gradually ulcerate and enlarge Tubercle bacilli can usually be demonstrated in the discharge from the ulcers Histoplasmosis may cause ulceration of the tongue the lip or the pharynx There is usually involvement of adjacent nodes Diagnosis may be made by discovery of other evidence of the disease or by local biopsy In typhoid fever ulcerations of the mouth are not uncommon They are associated with other manifestations of the disease The lesions of herpes simplex activated by other infectious diseases such as pneumonia epidemic meningitis *etc* may be characterized by vesicle formation and subsequent ulceration the lesions appearing on the lips under the tongue or at the base of the alveolar processes Ulcerative stomatitis may occur in children or in adults and seems to be associated with general dietary deficiency and such local devitalizing factors as dental sepsis It is accompanied by swelling and hyperemia with subsequent necrosis and ulceration along the border of the gums and extension of that necrosis and ulceration to the cheek

and lower side of the tongue. It may progress to gangrenous stomatitis or noma. Treatment consists in providing an adequate diet, taking care of carious teeth or necrotic bone, prescribing mouth washes, and administering antibiotics. Gangrenous stomatitis may be fatal unless treated adequately in its early stages. A specific form of ulcerative stomatitis is caused by a mixed *infection due to a fusiform bacillus and a* spirochete. In a typical case the organisms may be easily obtained from a smear of the lesions. In severe cases, this disease, which is known as trench mouth, may be accompanied by fever and constitutional symptoms. An initial hyperemia of the gums is followed by the formation of a dirty membrane and the appearance of patches on the tongue, the cheeks, the palate, and the tonsils. Penicillin therapy is highly effective. Ludwig's angina is due to an acute streptococcal infection involving the floor of the mouth. There are marked constitutional symptoms. Local swelling is striking and the disease is frequently fatal unless energetic treatment is carried out. Therapeutic measures must be prompt and include surgical incision and drainage—tracheotomy if necessary—and the prompt use of chemotherapeutic or antibiotic agents. Diphtherial infection is rarely found about the mouth and tongue. The diphtheritic membrane may extend from the throat to the pharynx and palate and may be an important cause of local symptoms. Specific treatment by the use of a concentrated preparation of the diphtheria antitoxin is obviously the therapy of choice. It should be pointed out that spontaneous bleeding from the gums or the buccal mucous membrane may be a striking manifestation of other diseases, such as thrombocytopenia, due to any cause, the leukemias, or to the hypoprothrombinemia associated with liver disease or chronic diarrheas.

*Neoplasms.*—Cancer of the oral cavity is the cause of approximately 5 per cent of all cancer deaths. It is most common in males. It is usually encountered in the later decades. Involvement of the lip is the most common but carcinomatous disease of the tongue and cheek is not rare. The diagnosis should be suspected if there are the local manifestations of leukoplakia, an indolent ulcer, a papillomatous or nodular tumor, or evident infiltration around a fissure. Successful treatment depends upon early diagnosis and a determination of the type or location of the tumor. If the disease is suspected, biopsy material should be obtained, preferably with the use of electrocautery. Radiotherapy or radical surgery is the only measure to be employed. Other tumors about the mouth include epulis, a fibrous tumor of the gum, ranula, a cyst due to obstruction of the ducts of the mucous or salivary glands under the tongue, and torus palatinus, an exostosis of the palatal processes of the maxilla presenting as a mass in the roof of the mouth. Surgical removal should be carried out in each instance.

*Buccal Changes Due to Noxious Substances.*—Discoloration of the gums may be associated with the toxic effects of bismuth or lead. The bismuth line is located at the gum margin as a series of fine punctate dots of a bluish black color. It is less sharply defined than that associated with lead poisoning. In the case of bismuth, punctate or diffuse pigmentation may occur on the cheeks or the soft palate; occasionally stomatitis or gingivitis, with severe ulceration, may be encountered. Mercury poisoning as a result of therapy or of occupational hazards may result in swollen, tender gums which bleed easily. The local lesions may progress to actual ulceration, with loosening of the teeth and necrosis of the jaw. Dilantin (sodium phenylhydantoinate) may cause soreness and bleeding of the gums, later followed by marked hypertrophy until the teeth are nearly covered. Such an extreme degree of hypertrophy may cause difficulty in chewing and limitation of various dietary factors. Withdrawal of the toxic substance usually results in complete clearing of the local toxic manifestations. Occasionally local surgical measures, or even the treatment of secondary infection, may be necessary. Pigmentation of the gums and cheeks may be associated with other substances, such as silver or arsenic, and may be characteristically observed as a result of adrenalin insufficiency, as seen in Addison's disease.

## DISEASES OF THE ESOPHAGUS

Disease of the esophagus can usually be diagnosed on the basis of a careful history Furthermore because of the fairly accurate localization of pain or discomfort from different levels of the esophagus the site of pathological change or disturbance can frequently be determined with reasonable accuracy The exact nature and location of esophageal disease can only be clarified by careful roentgenologic examination and by esophagoscopy with suitable study of biopsy material

Substernal discomfort or pain as already noted is characteristic of esophageal disease It may go into the back or may spread into one or both arms simulating angina or it may radiate into the neck and postauricular area There is practically always a close relationship between the ingestion of food and the appearance of symptoms The nature of esophageal symptoms varies greatly Intense substernal burning (heartburn) is usually associated with abnormal esophageal function with regurgitation of gastric contents into the lower end of the esophagus or with local smooth muscle spasm at or near the cardia Severe cramping pain may occur in the absence of structural disease but as a rule intense local spasm is associated with developmental abnormalities which act as trigger points for the stimulation of increased motor activity It may also be associated with actual ulceration of the esophagus which ordinarily is to be found in the neighborhood of the cardia Another type of symptom is that of difficulty in swallowing or a feeling of constriction at a certain point beyond which ingested material passes with difficulty Such a symptom suggests obstruction and may be associated with the regurgitation of undigested food In the presence of an esophageal pouch or diverticulum of any magnitude food stasis may occur with putrefaction which results in a foul odor to the breath and the periodic regurgitation of putrid material In the presence of a gradually stenosing lesion a patient almost invariably complains of inability to pass food beyond a certain point This difficulty is first noted in relation to the ingestion of solid foods and eventually may even preclude the successful swallowing of liquid material except in very small quantities Any striking degree of dilatation of the esophagus always implies prolonged duration of the underlying condition With extreme dilatation, there is relatively little likelihood that pain will be a presenting symptom because of the stretching or atony of the esophageal musculature Symptoms associated with obstruction and marked dilatation are therefore characterized by substernal fullness without pain and difficulty in the passage of food beyond a certain point It is obvious that esophageal symptoms of long duration will almost invariably be accompanied by malnutrition of a major degree because of the difficulty in ingesting an adequate amount of food

Physical examinations in patients suffering from esophageal disease may provide evidence of cervical or mediastinal pressure tracheal displacement, metastatic cervical nodes neurological abnormalities and signs of malnutrition It rarely provides direct evidence of esophageal disease

Abnormalities of the esophagus may be classified as follows

1 Motor Disturbances
2 Developmental Abnormalities
3 Neighborhood Disease (Extraluminal)
4 Inflammatory or Traumatic Disease (Intraluminal)
5 Degenerative Disease
6 Neoplastic Disease
7 Esophageal Varices

*Disturbances of Motility* —The most common manifestation of a motor disturbance is heartburn It is frequently encountered in the early months of pregnancy and in hyperreactive individuals The symptom is apt to follow the too-rapid ingestion of food the taking of food when tense or fatigued or the excessive use of tobacco In the absence of structural disease it is usually relieved by regulation of habits or by the use of antacids or antispasmodics Intractable heartburn should suggest the possibility of definite organic disease either in the esophagus or in the stomach duodenum or gallbladder

and lower side of the tongue It may progress to gangrenous stomatitis or noma Treatment consists in providing an adequate diet, taking care of carious teeth or necrotic bone prescribing mouth washes, and administering antibiotics Gangrenous stomatitis may be fatal unless treated adequately in its early stages A specific form of ulcerative stomatitis is caused by a mixed infection due to a fusiform bacillus and a spirochete In a typical case the organisms may be easily obtained from a smear of the lesions In severe cases this disease which is known as trench mouth, may be accompanied by fever and constitutional symptoms An initial hyperemia of the gums is followed by the formation of a dirty membrane and the appearance of patches on the tongue, the cheeks, the palate and the tonsils Penicillin therapy is highly effective Ludwig s angina is due to an acute streptococcal infection involving the floor of the mouth There are marked constitutional symptoms Local swelling is striking and the disease is frequently fatal unless energetic treatment is carried out Therapeutic measures must be prompt and include surgical incison and drainage—tracheotomy if necessary—and the prompt use of chemotherapeutic or antibiotic agents Diphtherial infection is rarely found about the mouth and tongue The diphtheritic membrane may extend from the throat to the pharynx and palate and may be an important cause of local symptoms Specific treatment by the use of a concentrated preparation of the diphtheria antitoxin is obviously the therapy of choice It should be pointed out that spontaneous bleeding from the gums or the buccal mucous membrane may be a striking manifestation of other diseases, such as thrombocytopenia due to any cause the leukemias or to the hypoprothrombinemia associated with liver disease or chronic diarrheas

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FIG 196 —Achalasia of the cardia Note fusiform narrowing and symmetrical mucosal markings

gastrostomy with resection of the stenosed lower end of the esophagus may have to be performed

*Developmental Abnormalities* —These include congenital atresia of the esophagus with tracheo esophageal fistula esophageal webs diverticula congenital short esophagus and paraesophageal hernia

Total regurgitation of food and an aspiration pneumonia in the newborn infant are the cardinal diagnostic points of congential atresia of the esophagus with tracheo esophageal fistula It can be treated with some chance of success if a skilled thoracic surgeon is available

Esophageal webs represent redundant folds of mucous membrane capable of causing obstructive symptoms Identification of the condition is made by esophagoscopy and treatment consists in rupture of the web and subsequent bouginage

Diverticula are of two types pulsion diverticula and those due to external traction The former are typically to be found at the pharyngoesophageal junction (an area inadequately protected by the cricopharyngeal muscle layers) and at the point where the left bronchus crosses the esophagus anteriorly and may cause pressure Pouches may also occur as the result of local injury as from a lye burn Symptoms depend upon the size of the pouch the amount of food stasis that occurs and in the case of a large diverticulum upon the fact that when full it may actually compress the adjacent segment of the gullet with consequent obstruction Localization of symptoms is usually remarkably accurate In the case of those diverticula at the pharyngo-esophageal junction the full pouch may form a mass easily noted by the patient in the supraclavicular region Small diverticula usually are symptomless unless they act as trigger points in disturbing normal motility in overreactive individuals Traction diverticula are lateral outpocketings as the result of an adjacent inflammatory cicatrizing process in the mediastinum They are usually small in size and of little importance except as noted above Diagnosis of diverticula is easily made by *x* ray Mild symptoms can be readily controlled by simple dietary measures When symptoms become prominent and cause severe pain due to local spasm or regurgitation of retained food surgical intervention becomes advisable and proper plastic measures can be carried out by the transthoracic route

Congenital short esophagus is relatively uncommon In this condition the stomach is pulled directly through the esophageal hiatus into the thoracic cavity There is frequently a development of actual gastritis in the herniated portion of the stomach and occasionally of peptic ulcer of the esophagus in the segment just above the cardia with more or less typical ulcer symptoms It will be discussed under inflammatory lesions

Hiatus hernia represents a developmental defect secondary to a large esophageal hiatus Symptoms may be entirely absent

Severe substernal pain secondary to esophageal spasm may at times be sufficient to necessitate the occasional use of narcotics. When encountered, it should suggest the presence of abnormalities, such as esophageal ulcer, diverticulum or hiatus hernia. In the absence of structural changes treatment should be directed toward control of emotional disturbances, regulation of diet, avoidance of rapid eating and restriction in the use of tobacco and alcohol. The use of atropine or similar antispasmodics before the ingestion of food may be very helpful. Immediate relief of pain may be procured by the use of nitroglycerine and occasionally by the sipping of a hot solution of bicarbonate of soda. Functional dysphagia and globus hystericus may occur in emotionally unstable persons of either sex. The most prominent symptom is a fear of choking following the ingestion of either solid or liquid foods. The diagnosis of these nervous manifestations is untenable unless the possibility of more serious organic disease of the esophagus has been ruled out by careful esophagoscopic examination.

Local neurological disease such as bulbar palsy secondary to tabes or any other disease of the central nervous system may produce swallowing difficulties. Similarly, myasthenia gravis may make swallowing difficult or impossible as the result of fatigue of the pharyngeal muscles.

Achalasia of the cardia or so-called cardiospasm presents a different type of clinical picture. This condition is usually encountered in young neurotic individuals. As the term implies, there is failure of relaxation of the lower segment of the esophagus just above the cardia with resulting difficulty in the passage of food and secretions into the stomach. The fundamental cause is not entirely clear. It may be due to degeneration or absence of the ganglion cells in Auerbach's plexus in the terminal segment of the esophagus or theoretically it may be caused by inadequate or vestigial control of this segment by the vagus nerve. In any event there appears to be a functional overstimulation of the cardiac segment by sympathetic stimuli with resulting failure of normal relaxation. A curious and rare condition that is almost indistinguishable from the above condition is associated with hypertrophy of the esophageal musculature just proximal to the cardia with resulting "cardiospasm." In either case gradual dilatation of the esophagus results. Over the years there is an associated local esophagitis secondary to the stasis of food and secretions. This is initially marked by swelling and local congestion and subsequently fibrotic thickening, with permanent constriction of the lumen. X-rays of the esophagus show varying degrees of dilatation and tortuosity, with a smooth, symmetrical fusiform narrowing at the lower end. Esophagoscopy will characteristically show varying degrees of esophagitis in the lowest portion, occasionally with minute superficial erosions. Initial symptoms of achalasia are those of substernal fullness, but as the disease progresses symptoms of obstruction develop with dysphagia and regurgitation of food. The latter characteristically occurs at night and may produce an aspiration pneumonitis. Symptoms are aggravated by emotional tension, hurried eating and the ingestion of bulky or very cold foods. Remissions are frequent in the earlier months or years of the condition. When dysphagia is a prominent symptom it may be accompanied by severe malnutrition. Diagnosis is readily established in most instances by *x*-ray examination of the esophagus. The possibility of esophageal cancer must never be forgotten, and when persistent narrowing has occurred, esophagoscopy with a biopsy from the stenosed area is frequently indicated. Treatment obviously depends upon the stage of the disease. In the early stages treatment consists in the proper handling of emotional difficulties and regulation of diet and eating habits. Bulky, irritating or extremely cold foods should be avoided, as should alcohol and tobacco. The use of nitrites before the ingestion of food is frequently of great help. In the later stages of the disease careful bouginage at regular periods may alleviate the symptoms and permit an adequate food intake. It should only be carried out by an experienced endoscopist. If attempts to relieve symptoms by the passage of bougies or of dilating bags is not successful, then resort to surgery may be necessary. In this event an esophago-

with an acute inflammatory process involving the interior and exterior surfaces Such traumatic accidents if not immediately fatal may subsequently produce cicatricial strictures with varying degrees of obstruction The acute reactions to trauma may include mediastinitis with fever leukocytosis *etc* Treatment here consists in the careful feeding of bland foods provided emergency surgery is not indicated and the use of antibiotics Residual strictures require the use of guided bougies and rarely resection of stenosed areas and anastomotic surgery

Specific granulomatous diseases such as syphilis and tuberculosis rarely cause local ulceration, cicatrization and stenosis with accompanying obstructive symptoms Scleroderma may be the cause of multiple irregular constricting lesions in the esophagus The diagnosis in each instance is made by recognition of other manifestations of the disease in question

Peptic ulcer of the esophagus may occur It is likely to appear in the congenital short esophagus possibly because of the easy regurgitation of gastric juice that occurs in this condition The ulcer is found near the cardia and produces symptoms of two types one is characteristic of ulcer in general—pain after eating relieved by food or antacid the other is essentially esophageal and is due to the associated spasm which may in itself cause severe intractable pain and dysphagia With recurrent attacks, stenosis of the esophagus typically develops with frank obstruction Diagnosis is made by radioscopic examination or by direct endoscopy If routine measures employed in the treatment of peptic ulcer are not effective the disease may progress until sufficient obstruction exists to warrant resection and esophagogastrostomy In general it may be said that the condition is extraordinarily difficult to handle Complications are those of peptic ulcer elsewhere It should be mentioned that peptic ulceration of the esophagus is not infrequently associated with gastric or duodenal ulceration

Acute esophagitis not only may be associated with trauma from various causes but may also accompany an acute infectious disease such as diphtheria, smallpox typhoid or thrush It is of course a serious complication Chronic esophagitis may be the commonest disease of the esophagus In the majority of instances it is directly related to other diseases of the digestive tract especially to those in which vomiting or regurgitation of acid gastric secretions is of frequent occurrence Many cases have been noted in association with hiatus hernia esophageal ulcer, duodenal ulcer and in recent years, esophagogastrostomy It eventually produces shortening and stricture at or near the esophagogastric junction causing dysphagia and regurgitation usually without nausea or real vomiting Heartburn is common and inability to belch is frequently noted Diagnosis is by *x* ray examination and esophagoscopy Once the possibility of malignancy in the stricture is eliminated successful therapy usually can be obtained by careful dilatation with a string guided bougie If dysphagia is unrelieved by this means resection of the stricture and esophagogastrostomy is indicated

*Degenerative Disease* is associated with atrophic changes in the esophageal mucosa and is encountered in such conditions as pellagra the Plummer-Vinson syndrome pernicious anemia and other similar deficiency states The substernal burning encountered in pellagra responds readily to niacin therapy Adequate iron therapy may relieve esophageal symptoms encountered in the Plummer Vinson syndrome whereas the use of liver or vitamin $B_{1}$ will readily improve the occasional esophageal symptoms encountered in pernicious anemia

*Neoplastic Disease* of the esophagus is most frequently carcinoma Other malignant or benign tumors occur but are numerically of minor importance The majority of esophageal cancers involve the lower and mid portions and are either squamous-cell (esophageal) or adenocarcinomatous (gastric) in character Symptoms are essentially those of an obstructing lesion Early in the course of the disease substernal pain may be present but as a rule difficulty in swallowing loss of appetite and malnutrition are the characteristic symptoms with later regurgitation excessive thirst and constipation of marked degree Bleeding usually of

even when the herniation of the stomach through the esophageal hiatus is readily apparent by *x*-ray examination When symptoms are present they are characterized by high epigastric distress, probably secondary to localized gastritis in the herniated portion of the stomach, or by substernal distress, dysphagia or regurgitation, particularly in the recumbent position, and severe heartburn In patients who have symptoms from a hiatus hernia, anemia secondary to moderate bleeding is not uncommon and gross hematemesis may occur Symptoms are usually not noted before the age of 40 At times, distress associated with hiatus hernia is distinguished with difficulty from symptoms due to coronary heart disease inasmuch as the pain may radiate to one or both shoulders and down the arm Like the pain of angina pectoris the symptoms may be aggravated by emotional tension and overeating It is usually not related to exertion however, and is made worse rather than relieved by the ingestion of alcohol The diagnosis by roentgenologic examination is easy if symptoms are suspected It should be noted that diverticula of the colon duodenum, or small intestine are frequently encountered in association with hiatus hernia It should also be noted that, at times diagnostic difficulties arise because of coexisting coronary heart disease or the presence of cholelithiasis Treatment comprises the use of frequent small feedings of non irritating food, the use of antispasmodics and antacids, and simple but intelligent psychotherapy If symptoms become intractable or if major bleeding occurs, transthoracic surgical repair of the hernia is necessary and will usually be accompanied by an excellent result

*Neighborhood Disease* is associated with mediastinal tumors aneurysm of the aorta metastatic disease causing enlargement of mediastinal glands extreme cardiac enlargement or pericardial effusion (rare) and occasionally inflammatory disease of the diaphragmatic pleura which may cause esophageal compression or irritation The cause of symptoms is usually apparent on radioscopic examination Therapy should be directed toward the primary disease

*Inflammatory Disease or Traumatic Disease* involving the esophagus usually is intraluminal Perforation of the esophagus by instrumentation ingested foreign bodies or caustics or rupture of the esophagus by excessive vomiting may be associated

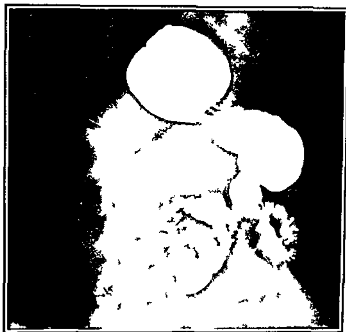


FIG 197 —Hiatus hernia About one third of stomach above curve of diaphragm

and such a diagnostic procedure is entirely justified if other methods fail to demonstrate the source of major upper gastrointestinal bleeding. Therapeutic measures will be discussed in a later section.

## DISEASES OF THE STOMACH

Gastric disturbances may be associated with abnormalities of motor or secretory function, developmental abnormalities, new growths, and with focal or diffuse inflammatory processes. Symptoms arising from the stomach are almost always referred to the epigastrium and may be described by such terms as fullness, distention, gas, heartburn, gnawing or burning pain. In addition, more general symptoms may be anorexia, nausea and vomiting. None of these symptoms is specific for any particular disease, but in general it can be said that periodic gnawing pain suggests local ulceration, that a steady burning or aching pain suggests a more diffuse inflammatory process such as gastritis, and that nausea and vomiting imply the probability either of a diffuse acute inflammatory process or of partial obstruction. In almost every instance symptoms are related to the intake of food, which may relieve or may aggravate the discomfort. Diagnosis of disease of the stomach depends primarily on a good history, which should include a careful analysis of eating habits, dietary adequacy, and the use of alcohol, tobacco, coffee, tea, and certain irritating drugs such as the salicylates and the newer antibiotics. Physical examination may reveal local distention, a palpable mass, or local tenderness as confirmatory evidence of gastric disease. Further definition of the type and location of gastric disease can be obtained by adequate roentgenologic examination or by gastroscopy. Gastric analysis rarely provides diagnostic material, at the best it gives evidence of excessive gastric secretion or true achlorhydria. In cases of obstruction it aids in measuring the degree of retention or of gastric emptying. Careful cytological studies of gastric residues properly obtained and stained with the Papanicolaou technique may prove the presence of malignant cells, but this method can only be utilized where the services of a highly trained technician are available.

Motor Disturbances.—*Gastric atony* may occur as an acute phenomenon resulting in marked dilatation of the stomach. It is accompanied by weakness, epigastric fullness, regurgitation, nausea and vomiting. There is usually striking electrolyte loss with dehydration if the condition persists for any period of time. Pain is not remarkable. The vomitus is large in amount and usually bile-stained, or it may be black in color; in the latter case it represents old changed blood. Examination reveals a rapid thready pulse, frequently with an accompanying sharp rise in temperature and respirations, and in severe cases with evidence of shock or collapse. The abdomen is soft, distended, and there may be a succussion splash in the epigastrium.

The condition usually occurs shortly after major operation or after obstetrical delivery. It may be encountered in severe diabetic coma. If not recognized and treated energetically, it may result in coma and death. Treatment consists in gastric lavage and parenteral replacement of fluids and electrolytes. Aspiration frequently yields as much as from 3,000 to 4,000 cc. At times several aspirations may be necessary in order to restore tone to the gastric musculature. Following such an occurrence, feeding must be limited to very small amounts at a time. Postoperative gastric suction serves to prevent the development of acute dilatation of the stomach in most instances.

Atony of the stomach may occur in general debilitating diseases. Under such conditions its onset is very gradual, and a diagnosis is made only after careful observation and demonstration of gastric stasis without evidence of organic obstruction. It may also occur as a result of gradually increasing pyloric obstruction due to stenosing lesions. Under these circumstances it will almost invariably be associated with vomiting of increasing amounts of food. X-ray examination will show a dilated atonic stomach which should be treated by repeated aspirations or constant suction plus parenteral replacement of fluids and electrolytes. Ultimately, the pyloric obstruction must be treated surgically. The large, sagging stom

a minor degree may occur. An early diagnosis must depend upon an awareness of the significance of substernal distress in relation to the intake of food and anorexia. Roentgen ray studies, especially in older patients, are always warranted. It should be noted that in certain instances, obstructive symptoms associated with an obvious esophageal constriction may have been present for a long time. Barium studies may show an irregular lesion or occasionally a symmetrical narrowing. Esophagoscopy should be performed for the purpose of obtaining biopsy material from the stenosed area. The esophagoscopist should be prepared *to dilate* the constriction by means of a guided bougie in order to obtain an adequate biopsy from the center *of the* stricture.

Radical resection is dangerous and cure is infrequent especially in the later decades but skilful surgery may produce palliation from the distressing dysphagia *for two or* more years in a reasonable number of patients. In inoperable cases, intensive radiation at times produces extraordinary temporary results, and complete relief of dysphagia can frequently be obtained by careful dilatation of the constricted area by guided bougies.

The other benign or malignant tumors of the esophagus are less common than carcinoma and involve the same diagnostic and therapeutic considerations.



Fig 198.—*Cancer of the esophagus. Note irregular asymmetrical narrowing below dilatation*

*Esophageal Varices* are a common manifestation of any condition causing portal hypertension. They are entirely asymptomatic until gross hemorrhage occurs. Demonstration of esophageal varices can be provided by careful roentgen ray studies. Occasionally the presence of esophageal varices may be suspected but *x* ray demonstration may be difficult or impossible. Under such circumstances they may be readily recognized by careful es... py,

mal functioning Demonstration of gastroptosis or visceroptosis in a patient with symptomatic complaints should direct attention to that type of therapy which is chiefly concerned with the regulation of living habits and emotional difficulties

*Diverticula* of the stomach are either congenital or secondary to pulsion or traction They are relatively uncommon and they are usually seen in the region of the cardia Diagnosis is practically always an accidental one and is made in the course of a routine *x* ray examination Symptoms from gastric diverticula are rare but local inflammation may occur with epigastric discomfort or pain in relation to the intake of food In those instances in which a gastric diverticulum is secondary to traction from neighborhood disease relief of symptoms can be obtained only by treating the primary condition In rare instances in which the diverticulum is fairly large with accompanying stasis of food surgical excision or invagination of the diverticulum may be required

At this point it should be noted that diverticula may frequently occur in the duodenum and in the remainder of the small intestine Duodenal diverticula are fairly common and are usually found by accident in the course of a routine roentgen ray examination They rarely cause symptoms Occasionally they become the seat of an inflammatory process and cause epigastric distress and fullness Under these circumstances symptoms as a rule occur after a big meal and more particularly during the night The symptoms probably are due to faulty emptying of the diverticula and this can be demonstrated by giving a swallow of barium at bedtime and then *x* raying the patient while still in the horizontal position the first thing in the morning If there is marked stasis of barium then one may assume that symptoms are associated with the diverticulum and a program of small frequent feedings with particular reference to the evening meal may be of real help Diverticula in the first portion of the duodenum are of the traction variety and more frequently associated with duodenal ulcer Jejunal and ileal diverticula are usually asymptomatic but occasionally they are very numerous and may cause a sprue like picture with steatorrhea macrocytic anemia and general malnutrition

*Hiatus hernia* has been discussed in a previous section It may occur in association with the protrusion of other abdominal viscera through the diaphragm but it is more commonly encountered as the so-called paraesophageal hernia Where symptoms warrant surgical intervention operative repair of the hernia can best be accomplished by the transthoracic route and in skilled hands this operation has a very low mortality rate, probably under 2 per cent The herniation usually is the result of a developmental abnormality in the diaphragm but it may be the result of trauma to the diaphragm from a severe blow In the latter case surgical repair is usually indicated

*Hypertrophic stenosis* of the pylorus consists in obstructive narrowing secondary to hypertrophy of the pyloric muscle It most frequently occurs in newborn infants It may gradually develop in adults and under these circumstances, may be associated with an ulcerative process in the vicinity of the pyloric end of the stomach Symptoms in infants occur most frequently within a few weeks of birth but they may be noted as late as several months after delivery The condition occurs three or four times more frequently in male children than in female children In infants the pyloric region is found to consist of a mass of thickened muscular tissue that is extremely hard and involves an area 2–3 cm in length There is no evidence of inflammation The symptoms which are characteristic are persistent projectile vomiting loss of weight constipation and dehydration Physical examination typically reveals a distended globular stomach with easily visible peristaltic waves proceeding from left to right after the intake of food Occasionally a small rounded tumor may be palpated in the region of the pylorus if the child is sufficiently relaxed Easy confirmation of the diagnosis can be obtained by a barium swallow Initial treatment consists in sedation with small subcutaneous doses of sodium phenobarbital with or without the addition of very minute doses of atropine Small frequent feedings of breast milk or prepared milk with a very fine curd should be used If such conserva

ach seen in visceroptotic individuals is not an example of gastric atony and very rarely gives rise to symptoms

*Local spasm* of the stomach may occasionally be encountered in the presence of focal ulcerating lesions Segmental spasm may also be seen in conditions, such as tabes dorsalis and other similar diseases of the spinal cord, and may occasionally be encountered in lead poisoning Where spasm is intense, it is associated with the production of pain

*Nervous vomiting* is indirectly an example of disturbed gastric motility secondary to profound psychiatric difficulties It is characterized by frequent effortless vomiting of portions of meals, without nausea and without loss of weight Although the patient complains constantly of vomiting, careful history almost always brings out a story of emotional difficulties that may be in the nature of true hysteria or of other typical neurotic manifestations Careful *x* ray examination is often indicated in order to rule out organic disease Once the identity of the problem is apparent, psychotherapy offers the only source of relief It is not always effective

SECRETORY DISTURBANCES —Variations in the volume of gastric secretion or in the concentration of acid or pepsin cover a broad range and are frequently encountered in any group of normal individuals An increase or a decrease in gastric secretory activity can be readily produced by emotional factors as shown by Wolf and Wolff and by numerous other investigators Fear may depress secretory activity to a very low level, and conversely anger and frustration may increase the volume and concentration of gastric secretions So-called hyperacidity and hypo acidity have little meaning and certainly have little or no relationship to the production of symptoms In general, it can be said that variations in secretory activity are not to be correlated with specific symptoms or diseases Two exceptions are chronic peptic ulcer and pernicious anemia The former is associated with hypersecretion and is practically never encountered in a continuing absence of gastric juice whereas patients with pernicious anemia rarely, if ever, show evidence of gastric acidity Total achlorhydria, with failure to respond to histamine stimulation, may occur in perfectly normal individuals The incidence of such a finding increases progressively with increase in age It may also be encountered in a high percentage of cases of gastric carcinoma and as noted above, in patients with pernicious anemia or combined degeneration of the spinal cord

*Achlorhydria* may occur as a result of chronic gastritis, with an ultimate, irreversible change in the gastric mucosa This change is an atrophic one and may also be encountered in certain deficiency diseases, in which it is more properly classified as gastric atrophy than as atrophic gastritis In the absence of free hydrochloric acid in the stomach, more rapid emptying of the organ obtains and it is possible that, occasionally so-called gastrogenic diarrhea may result from this secretory disturbance The proof of such an entity is not always readily obtained, and the diagnosis should not be made until other causes of diarrhea are excluded In the absence of other causes, seemingly intractable diarrhea usually in older people may be relieved by the use of adequate doses of dilute hydrochloric acid (U S P ) or glutamic acid hydrochloride taken with meals The diagnosis is never justifiable unless a demonstrated achlorhydria has been shown to be present in the absence of any other morbid condition of the alimentary tract

DEVELOPMENTAL ABNORMALITIES — *Visceroptosis* —For the most part developmental abnormalities are not productive of symptoms and do not require treatment Mention should be made of the term *gastroptosis* in relation to so called visceroptosis or Glenard s disease In this condition ptosis of the stomach occurs in association with a sagging position of most of the other abdominal viscera In all probability this condition should not be credited as being the cause of symptoms although much attention has been paid to it in the past Individuals with this condition are almost invariably of an asthenic build and symptoms are usually manifestations of an underlying neurasthenia The position of the stomach or for that matter of other abdominal organs rarely if ever seriously interferes with nor

widespread necrosis of the gastric mucosa if sufficient material passes the esophagus and still remains active when it reaches the stomach. An especially severe type of acute gastritis is that classified as phlegmonous gastritis. This type is due to a pyogenic infection, usually streptococcal in origin, which begins as a localized cellulitis and may develop into a circumscribed abscess or a diffuse phlegmon.

The symptomatology of acute gastritis ranges from that of nausea and vomiting with mild epigastric discomfort to extremely diffuse epigastric pain and local tenderness with severe vomiting, fever, dehydration and a septic course. In all but the most severe cases a diagnosis will be made on the basis of a history of marked dietary indiscretion, the ingestion of some corrosive substance or intercurrent infection immediately preceding the onset of symptoms. X-ray examination or gastroscopy is in most instances entirely unnecessary. Treatment consists simply in the administration of frequent small feedings of very bland foods, moderate sedation, and the use of antacids. If lye or some other corrosive substance has been swallowed, instrumentation of any sort should be avoided and the patient should be given only soothing liquids such as milk, egg albumen, thin jellies and the like. Once the acute symptoms have subsided, *x*-ray examination of the esophagus and stomach should be performed to determine the amount of injury that has resulted. The patient's course should be followed with care, inasmuch as healing is associated nearly always with cicatricial stenosis and frequently with obstruction either in the esophagus or in the stomach or both. If this occurs, careful dilatation by guided bougies or plastic surgery is indicated. Phlegmonous gastritis is rarely diagnosed preoperatively, but the intensity of the epigastric symptoms, the degree of local tenderness and the septic temperature may give an indication. The use of antibiotics is indicated and, if necessary, surgical intervention with drainage or resection.

*Chronic gastritis* has been classified in various manners and by the use of various descriptive terms. With the advance in our knowledge of this subject following the introduction by Schindler of the flexible gastroscope, a precise diagnosis is now possible, and in all probability the simplest classification is the best. That suggested by Benedict would seem to have particular merit because of its simplicity and because it corresponds adequately to the findings of the pathologist. This classification divides gastritis into three categories—superficial, hypertrophic and atrophic. The term *gastric atrophy* should be used to differentiate atrophy of the stomach secondary to deficiency disease from that due to a local or diffuse inflammatory process. The former is more or less completely reversible with adequate replacement therapy. Superficial gastritis may be found as a separate entity or combined with atrophic gastritis. Patchy areas of gastric atrophy may also be noted in combination with other forms of gastritis.

The *diagnosis* of gastritis may be suggested by the symptomatology presented by a given patient but can be definitely determined only by adequate gastroscopic observation. In many instances a diagnosis of hypertrophic gastritis can be suggested by the radiologist on the basis of thick mucosal folds and an increased secretion of mucus. Such a diagnosis is not conclusive, however, and striking instances have occurred in which an *x*-ray diagnosis of hypertrophic gastritis has been shown to be erroneous because of obvious gastroscopic findings of almost complete atrophy of the gastric mucosa. The gastroscopic picture in acute superficial gastritis is that of reddening, edema, and adherent secretions. Erosions are not infrequently seen, and areas of submucosal hemorrhage are common. The red edematous mucosa is easily traumatized with subsequent bleeding. Chronic hypertrophic gastritis characteristically presents a verrucous appearance of the mucosa, with obvious hypertrophy of the gastric folds. At times the warty elevations are so large as to suggest tumor formation, and differentiation between severe hypertrophic gastritis and an infiltrating tumor may be impossible. Under such conditions biopsy of the gastric mucosa through the operating gastroscope frequently provides diagnostic material. Atrophic gastritis and gastric atrophy present an endoscopic appearance of a very thin, smooth, pale-gray

tive measures fail to control symptoms and to permit adequate food intake then recourse must be had to surgical intervention This is accomplished by means of the so called Rammstedt operation a procedure *which divides the pyloric muscle longitudinally down to the mucosa* The operation is highly successful in competent hands if it is performed without undue delay

In adults, pyloric hypertrophy may represent the persistence of the congenital condition described above or may be associated with inflammatory disease such as gastric ulcer or gastritis In the absence of inflammatory disease the condition may be relatively asymptomatic or may be marked by periodic episodes of moderate nausea and vomiting which may increase in severity as time goes on Unless there is an associated lesion pain is not present The exact diagnosis of this condition is adults is difficult A preceding story of numerous episodes of periodic vomiting without pain may lead to the suspicion that the condition exists Roentgenologic studies may suggest the disease because of the abnormal width of the pylorus and dilatation of the stomach It may be impossible however, to differentiate this condition from a scirrhous type of carcinoma involving the pyloric end of the antrum Confirmatory evidence may be obtained occasionally by gastroscopic examination particularly if the pyloric end of the stomach is visible through the gastroscope and it is possible to obtain biospy material In the presence of gastric ulcer as will be subsequently discussed the first consideration is to reach the decision that the ulcerating lesion is benign *If any doubt exists or* if antral cancer can be demonstrated radical surgery is indicated with adequate gastric resection If the condition is associated with a benign gastric ulcer recurrences are to be expected in most instances and medical treatment over any period of time is relatively unsuccessful If pyloric hypertrophy alone is present simple pyloroplasty is indicated in the presence of persistent symptoms

Foreign Bodies —Foreign bodies to be found in the *stomach* range from pins tacks and nails to objects as large as knives, forks and spoons In most instances the foreign body has been swallowed by accident but occasionally, swallowing such an object is the act of a mentally unbalanced individual Most of the smaller objects are passed through the stomach and emerge in the stool without causing harm Occasionally however, sharply pointed objects may penetrate the wall of the stomach causing local bleeding or actual perforation with subsequent peritonitis When a history can be obtained of an accidentally swallowed foreign body the patient should be referred to a competent esophagoscopist at once and localization of the object should be obtained by fluoroscopy or *x* ray examination If a satisfactory passage of the object through the stomach into the alimentary canal does not occur then removal should be performed either by the endoscopist with special instrumentation or by gastrotomy

The most interesting foreign body is that known as a *bezoar* a large concretion which may be composed of hair plant fibers shellac or other substances The symptoms from such a concretion depend upon its size and the irritation that it may cause in the stomach itself Epigastric heaviness fullness pain or periodic vomiting attacks may occur Organic disease such as ulcer or neoplasm may frequently be mimicked by the presence of a bezoar in the stomach The diagnosis can be established by roentgenologic examination because of the finding of a large filling defect which is freely movable and ordinarily located in the antrum Gastroscopic examination may demonstrate the nature of the mass Treatment consists in gastrotomy Complications of this condition will be those of either ulceration or obstruction

Inflammatory Diseases of the Stomach —*Gastritis* is undoubtedly the commonest disease of the stomach It frequently appears as an *acute* manifestation due to mechanical irritation by coarse foods overeating or overindulgence in alcohol or it may be produced by specific infectious diseases notably diphtheria scarlet fever and measles in children and influenza in adults It may also result from irritating drugs such as aspirin nicotine caffeine and the like The corrosive effect of such substances as lye and cresol which have been swallowed by accident or with suicidal intent may produce

widespread necrosis of the gastric mucosa if sufficient material passes the esophagus and still remains active when it reaches the stomach. An especially severe type of acute gastritis is that classified as phlegmonous gastritis. This type is due to a pyogenic infection, usually streptococcal in origin, which begins as a localized cellulitis and may develop into a circumscribed abscess or a diffuse phlegmon.

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mucosa through which blood vessels are easily visible Gastric rugæ are absent Atrophy may be complete or it may be patchy In complete atrophy there is histamine achlorhydria

The *symptomatology* of chronic gastritis is not characteristic Epigastric distress nausea, vomiting hemorrhage, loss of weight, etc may be encountered In many instances aside from nutritional disturbances patients complain of few or no symptoms referable to the stomach At times, the history is that of a rather atypical ulcer or gastric cancer At other times, epigastric discomfort and accompanying symptoms may seem to be entirely independent of food and unrelieved by antacids It should be pointed out that, frequently superficial gastritis and at times hypertrophic gastritis are seen in association with peptic ulcer of the stomach or duodenum

Once the diagnosis of gastritis is established, *treatment* may be instituted on the basis of a general program of careful regulation of eating habits with the institution of small regular feedings of bland food eaten slowly and on time Excessive smoking should be avoided, as should the use of alcohol tea and coffee Simple medication such as aluminum hydroxide antacid preparations mild sedation with the barbiturates, and antispasmodics, is frequently of assistance in controlling symptoms In cases in which there is complete gastric atrophy and histamine achlorhydria it is important to rule out such conditions as primary pernicious anemia and (occasionally) nontropical sprue Infrequently patients with gastric atrophy are encountered who do not have either of the above conditions but whose symptoms are those of anorexia loss of weight, vague epigastric distress and moderate anemia unaccompanied by evidences of bleeding These patients respond in a rather dramatic manner to prolonged therapy with liver extract and the gradual administration of a thoroughly adequate diet It has been shown that regeneration of the mucosa may occur under such therapy, as may occasionally be the case in pernicious anemia although gastric secretory changes are seldom if ever, restored, to normal

Special mention should be made of those who present themselves with a story of acute massive gastric hemorrhage with few if any other symptoms In such cases, the obvious duty of the physician is to rule out structural disease, such as peptic ulcer, cancer esophageal varices, and hiatus hernia as the source of bleeding Once this has been done careful gastroscopy is indicated and may provide the necessary explanation and diagnosis Not a few such cases may bleed massively, even to shock levels, solely on the basis of severe superficial gastritis with extreme hyperemia and numerous erosions The cause of such a condition is usually obscure, but, occasionally, a careful history will reveal the excessive use of alcohol or the chewing of such substances as snuff or tobacco with constant swallowing of the irritating material On occasion the continued use of aspirin may produce a similar picture When such a history can be obtained, careful dietary regulation and the elimination of the irritating substance may produce satisfactory regression of the gastric irritation and obviate further serious bleeding Inasmuch as patients may occasionally have a fatal hemorrhage as a result of gastritis of this degree, it is necessary to stress the importance of adequate gastroscopic examination if *x* ray studies are inconclusive or negative It may be mentioned that, occasionally, carefully planned medical regulation fails to control the situation and to prevent repeated episodes of bleeding In these rather rare instances subtotal gastrectomy may be necessary in order to obtain eventual control of dangerous hemorrhage

Finally a note of warning should be given as to the validity of the gastroscopic diagnosis of mild gastritis in the hands of inexperienced gastroscopists Temporary hyperemia hypersecretion, and irritability of the gastric mucosa can and frequently do occur as the result of nervous tension or emotional disturbances This was originally noted by Beaumont and has been brilliantly confirmed by Wolf and Wolff Erroneous diagnoses based on superficial transitory changes in the gastric mucosa are still too common and form the basis of unnecessary and often unwise therapeutic programs without benefit to the patient

Specific Inflammation of the Stomach—This type of inflammation may be due to a granulomatous process secondary to syphilis tuberculosis or such rare conditions as actinomycosis and other rare fungus infections

*Syphilis* may occur as a solitary gumma or as numerous gummatous lesions It may also be present as a diffuse nodular infiltrating process or as chronic fibrosis Symptoms are not sufficiently characteristic to suggest the diagnosis but most frequently simulate peptic ulcer or carcinoma with epigastric distress and marked loss of weight Hemorrhages rarely occur The diagnosis is essentially one of exclusion inasmuch as syphilis may occur coincidentally with peptic ulcer or cancer The radiological findings are not diagnostic but may simulate benign gastric ulcer carcinoma of the pylorus and antrum or diffuse scirrhous carcinoma (leather bottle stomach) Achlorhydria may be present and when found in the presence of an ulcerated lesion and positive serology, it should direct attention to the possibility of syphilis or cancer rather than to that of benign peptic ulcer Gastroscopic examination will readily demonstrate lesions of syphilis in the stomach but will not give a definitive answer In general it can be said that gastric syphilis should be given consideration in all cases in which patients have positive serological tests and demonstrable gastric lesions One added point is that except for symptoms of obstruction most gastric syphilis causes symptoms that appear to be of minor severity in relation to the lesion that has been demonstrated

*Treatment*—Where gastric syphilis is suspected routine antiluetic therapy should be instituted Failure to respond to such treatment should lead to the conclusion that the suspected lesion is probably carcinomatous

*Tuberculosis* of the stomach is usually a manifestation of late or terminal pulmonary tuberculosis In all but a few instances gastric tuberculosis is manifested by the presence of ulcerating lesions although an infiltrative type is recognized Symptomatically there is no characteristic clinical picture and a positive diagnosis can be made neither by *x* ray nor by gastroscopy The actual demonstration of tubercle bacilli in the lesions by direct biopsy is the only means of final identification In most instances treatment is symptomatic, but occasionally the general condition of the patient may warrant surgical intervention with local gastric resection

## PEPTIC ULCER

Although the diagnostic and therapeutic approach to the problem of gastric ulcer differs radically from that involved in peptic ulceration of the duodenum it will be convenient to discuss in general the problem of peptic ulcer involving either segment of the digestive tract As the term is clinically used peptic ulcer represents a chronic recurrent circumscribed ulceration of the gastric or duodenal mucosa To date it represents an essentially incurable condition The exact incidence of peptic ulcer is not known but autopsy evidence suggests that it may occur in 10 per cent of all people There is no particular racial predominance but it is four times more frequent in men than in women As a clinical entity it is much more frequently encountered in the duodenum than in the stomach but on the basis of autopsy statistics gastric lesions are more frequent than duodenal The malady may occur at any age from infancy into the late decades it is most common between the ages of twenty and thirty Although the typical ulcer patient is described as a slender asthenic individual it is not at all uncommon to encounter peptic ulcers in stocky somewhat overweight individuals As suggested above most peptic ulcers occur in the stomach or duodenum They may also occur at the cardiac end of the esophagus in the small bowel near the stoma of a gastroenterostomy or opposite the mouth of a Meckel s diverticulum In the stomach the vast majority of benign ulcers occur along the lesser curvature In the duodenum they are most frequently encountered in the first portion, the duodenal bulb Benign gastric ulcers may occur near the cardia along the greater curvature and not infrequently in the prepyloric region or at the pylorus Although usually single multiple ulcers are not uncommon They may occur concomitantly in the stomach or duodenum

or as so-called 'kissing' ulcers on the anterior and posterior walls of the duodenum. The actual size of the ulcerated area varies tremendously in diameter and depth. It always involves the muscularis mucosae and may *penetrate through the deeper layers* producing a complete perforation. The border of the ulcer is sharp, the floor of the ulcer is clean, and the surrounding mucosa may be normal or may show evidence of gastritis. Benign peptic ulcer is rarely seen in the presence of cancer of the stomach, but the presence of a benign ulcer either in the duodenum or in the stomach does not preclude the possibility of an independent malignant lesion. Peptic ulcer may occur in association with the development of brain lesions or following operation on them. No specific center in the brain seems to be particularly conducive to such an occurrence. During pregnancy, gastric or duodenal ulcer is rarely active.

*Etiology*.—The etiology of peptic ulcer is not known. Undoubtedly, acute ulceration of the stomach or duodenum may occur as the result of *local trauma* from the ingestion of irritating foreign bodies, or it may be associated with *severe burns*, in which case the lesion is known as a Curling's ulcer. Such an ulceration may be complicated by acute perforation or hemorrhage and sometimes may result in a chronic peptic ulcer. *Arterial infarction* or thrombosis may result *in local ulceration but as a rule the collateral* circulation is so adequate that this cause should not be overemphasized. With these exceptions, no satisfactory theory has been presented to date which adequately explains the causation of this common disease.



Fig 199.—Benign gastric ulcer. Note small rounded projection of ulcer crater in mid lesser curvature.

*Gastric hypersecretion* with an increased volume of gastric juice and an increase in gastric acidity is the usual finding in patients with peptic ulcer. In animals, peptic ulceration has been produced by the subcutaneous *injection of histamine and beeswax* with resulting overstimulation of gastric secretion for long periods of time. Various other animal experiments contribute definite evidence as to the importance of the lack of adequate neutralization of gastric digestive juice in the production of peptic ulceration. In human beings, however, proof is still lacking that increased secretion

alone as the cause of the disease. The nearest analogy is the occurrence of stomal ulcers following gastroenterostomy at a point in the mucosa of the jejunum where unneutralized gastric digestive juice is normally not present. Furthermore, it is an interesting fact that a subtotal gastrectomy which fails to remove the pyloric antrum is almost always followed by a stomal or jejunal ulcer, suggesting that the stimulus to excessive secretion was not adequately removed by the original operative procedure. Removal of the remaining antral segment almost invariably controls the situation at once.

*Neurogenic Concept.*—Cushing and others have called attention to the incidence of peptic ulcer in association with brain tumors and surgery for such conditions. The work of Wolf and Wolff has demonstrated the important role of emotional factors in relation to gastric secretory activity, and ulceration of the stomach has been produced by them as a result of slight trauma to the gastric mucosa and excessive nervous stimulation. The neurogenic concept of ulcer causation is indeed a fruitful source for careful consideration, but it must be admitted that this theory, too, fails to explain the etiology of the disease with entire satisfaction.

*Hormonal disturbances* have likewise been considered as an important, if not the most important, factor in the initiation of peptic ulceration. The fact that pregnancy seems to prevent the recurrence of duodenal or gastric ulcer in women is one of the bits of suggestive evidence leading to this type of investigation. Lack of protective mucus in the gastric secretion has also been proposed as an explanation for the occurrence of peptic ulceration.

Suffice to say that at present no single explanation is adequate to cover all—or indeed many—cases, and that all the various factors must be included in any consideration of the ulcer problem, either from the point of view of etiology or from that of therapy.

*Symptomatology.*—The classical symptom of peptic ulcer is epigastric gnawing or burning pain occurring at a measurable time after the ingestion of food and relieved by the taking of food or antacid. Pain or discomfort usually occurs anywhere from half an hour to two hours after the intake of food or in the early morning hours. In all parts of the world there seems to be a general tendency for ulcer symptoms to be more prominent in the spring or fall. Although the most constant symptom of ulcer is pain, it should be pointed out that in older individuals and in the presence of massive hemorrhage pain may be entirely absent. It should also be noted that in the early stages of peptic ulcer the usual periodicity in relation to food ingestion may be entirely lacking, and pain may occur during, immediately after, or at a prolonged period after the intake of food. As the course of the disease becomes more evident, the symptoms tend to fall into the usual pattern. In uncomplicated ulcer, symptoms may last from a few days to a few weeks and may be followed by complete remission of symptoms for many months or even years. In spite of prolonged remissions it must never be forgotten that the tendency of peptic ulcer is to recur. Additional symptoms are those of nausea and vomiting of greater or less degree. The occurrence of these symptoms always suggests probable obstruction at the pylorus. A further point in symptomatology is that epigastric pain may frequently be transmitted directly through to the back, usually at the level of the eighth dorsal vertebra, and on rare occasions may be experienced only at this level in the back. Under these circumstances the diagnosis may be suggested by the periodicity of pain occurrence.

The interval of time elapsing between the ingestion of food and the appearance of ulcer pain presents no essential difference in gastric ulcer as contrasted with ulcer of the duodenum. Although ulcer pain is typically located in the mid-epigastrium, it may frequently be experienced to the right or left of the midline, rarely in the lower abdominal quadrants. Jejunal ulcer typically produces pain in the periumbilical area at a level distinctly lower than that associated with either gastric or duodenal lesions. Back pain frequently suggests the possibility of deep perforation of either a gastric or a duodenal lesion with involvement of the pancreas, but such a deduction is not necessarily a

valid one At times the severity of the pain may be extreme and may be completely unrelieved by either food or antacid Under such circumstances, it is almost certain that one is dealing with a deep penetrating relatively intractable lesion

Any consideration of the mechanism of pain in peptic ulcer must include several factors, of which acid gastric juice and the existence of open mucosal ulceration are the two most important Local hyperemia and swelling and probably local muscle spasm are almost certainly contributing factors Patients with peptic ulcer as a rule have no abnormality of appetite and are usually well nourished, but loss of weight may occur as a result of pyloric obstruction or because of restriction of food intake due to fear of ulcer pain Constipation is common

*Diagnosis —Physical Examination* Diagnostic physical findings are usually not present but localized tenderness in the epigastrium over the site of the ulcer is not uncommon In the presence of pyloric obstruction a distended stomach may be observed and if retention is of sufficient degree a succussion splash may be elicited Very rarely, a *tender epigastric mass* may be made out The finding of such a mass should never be accepted as evidence of a benign ulcerating lesion It should always be considered *malignant until proved otherwise*

*Laboratory Examinations* The value of gastric analysis has already received adequate comment *As a diagnostic method,* it gives little information of value except as a means of determining the degree of gastric retention Achlorhydria in the presence of a gastric lesion should be accepted as an indication that the ulcerating lesion is malignant until it is proved otherwise by direct examination *The finding of blood in the gastric* contents or in the stool is of importance but is in no way diagnostic of the nature of the lesion



FIG 200 —Duodenal ulcer with typical clover leaf deformity

*Roentgenologic Examination* In peptic ulcer examination by a competent radiologist is the most important of all diagnostic procedures Approximately 95 per cent of all ulcers causing symptoms can be demonstrated roentgenologically As a rule the most difficult ulcer to demonstrate by *x* ray examination is the small posterior wall,

duodenal ulcer which may be entirely missed or which may be visualized only when the patient is examined in the right oblique position The demonstration of a gastric or duodenal deformity provides proof merely of previous ulceration with healing An explanation of the patient's symptoms at the time of the examination can be obtained only by the demonstration of an actual crater Stomal and jejunal ulcers are particularly difficult to demonstrate Failure to obtain conclusive *x* ray evidence of peptic ulceration in no way precludes the diagnosis Indeed the presence of a typical ulcer history in the absence of other findings is sufficiently suggestive to warrant a trial of ulcer therapy

In the presence of major bleeding with hematemesis or marked melena the decision to carry out adequate *x* ray examination is open to some controversy According to some the danger attending a meticulous radiological examination in the presence of active bleeding seems to preclude the use of such a procedure at that particular time The experience of many including the author would seem to indicate however that in the presence of unexplained major hemorrhage from the upper gastro-intestinal tract the risk associated with an *x* ray examination is far less than the danger of not being able to demonstrate the site of hemorrhage If the precaution is taken to avoid active manipulation of the epigastric area during roentgenologic examination adequate fluoroscopic and spot film technique may be carried out which will demonstrate the lesion responsible for the bleeding in a very high percentage of cases Such information is extremely valuable in the event that surgical measures may have to be considered and with the above precautions there should be no hesitation in ordering such studies

*Gastroscopic Examination* This diagnostic procedure has provided additional assistance in the difficult differentiation between benign and malignant ulcerations of the stomach and direct visualization will frequently provide an easy diagnosis The appearance of a benign ulcer has already been described A grossly malignant lesion is usually characterized by a dirty base possibly overhanging irregular margins nodularity and rigidity In doubtful cases, gastroscopic observation may yield no definitive information but the additional possibility of obtaining biopsy material under direct vision through an operating gastroscope may make an absolute diagnosis possible in an otherwise difficult case It should be noted that gastric ulcers may occasionally be missed by the gastroscopist because of the existence of certain blind areas in the stomach itself It is also true that the gastroscopist is occasionally able to demonstrate a gastric lesion that has previously escaped the radiologist

*Cytological Examination* A final addition to our diagnostic armamentarium is that of cytological study of gastric residues These can be obtained either by careful washing of the stomach and aspiration of the material through a nasal tube, or by aspiration of the material through a gastroscope When properly stained by the Papanicalaou technique confirmatory evidence of gastric malignancy can frequently be obtained Occasionally this diagnostic procedure is the only one to give definitive results short of surgical exploration

*Treatment — Medical* The therapy of peptic ulcer in general can be separated into two distinct phases The first is that of promoting healing of the acute lesion The second is that of preventing recurrence Except in the most intractable ulcers healing usually can be obtained in a relatively short space of time by standard procedures The time required for the healing of an acute ulcer varies particularly in relation to the age of the patient In the younger individual healing usually takes place in three or four weeks In the later decades of life final healing may be postponed for several months The absence of pain or distress gives no guarantee as to the completeness of the healing process In fact it is usually true that in the larger ulcers a crater may still be demonstrated days or weeks after symptoms have subsided

The essential therapeutic measures for the *healing of acute ulcers* are well recognized They consist in adequate rest both physical and mental the administration of small frequent feedings of extremely simple foods and the use of antacid preparations antispasmodics and sedatives Physical rest

may be obtained by putting the patient to bed either at home or in a hospital. Freedom from emotional tension is an equally or even more important consideration, however, and this can best be obtained by removing the patient from obviously tense situations and at the same time, using the *principles of good psychotherapy* to obtain relief from anxiety and from situations that are likely to cause frustration or resentment. The use of the *barbiturates will frequently* supplement such measures and may be very effective. Dietary measures to be used during the therapy of an active ulcer are best regulated by providing small hourly feedings of bland food containing protein or fat and given throughout the waking hours. During the night, the interval between feedings may be increased to two hours, but the feedings should be given regularly, even to the extent of waking the patient, at least for the first few days of treatment. Partial neutralization of gastric acidity may be obtained by the use of one or more of the various antacid preparations now available. It should be pointed out that mixtures of free alkalies which include bicarbonate of soda should be avoided in the presence of any evidence of renal disease, inasmuch as symptoms of serious alkalosis *may be rather easily produced*. In this connection, it is of interest to point out that occasionally, the prolonged use of an ulcer regimen, with a high milk content and the *liberal use of antacid preparations containing* bicarbonate of soda may eventually result in the formation of calcium stones in the kidneys. Furthermore mixtures containing magnesium *tend to produce* abdominal cramps due to excessive peristalsis and diarrhea, and those containing calcium carbonate may be productive of rather severe constipation. The newer *preparations containing* aluminum hydroxide may also cause constipation unless combined *with* magnesium trisilicate or mineral oil. In many instances, the use of antacids is *not necessary* to control ulcer symptoms, and there is little evidence that their use demonstrably accelerates the healing process. When ulcer pain is difficult to control, however, they *should* be used as a regular part of therapy. Atropine or its derivatives, or more recently banthine, a synthetic antispasmodic, is frequently of extreme value in helping to control the symptoms of an acute peptic ulcer. If either of these drugs *is used, it should be* employed in dosages just short of those *giving the unpleasant side-effects—dryness* of the mouth, blurring of the vision, occa*sional irritability and disorientation* and in older people difficulty in voiding. The latter complication must be particularly guarded against in very elderly individuals, inasmuch as *bladder* stasis may result, a very troublesome complication. Often a useful routine where the patient is emotionally disturbed and suffering a good deal of distress is the periodic use of hypodermically administered sodium luminal and atropine sulphate in proper doses. Such a measure given in sufficient doses may provide tremendous relief of emotional tension and enable the physician to get control of the ulcer situation. If such a routine is employed, care should be taken to avoid over sedation. Although the exact mode of action of banthine may differ somewhat from that of the atropine derivatives, the general principle is identical and the drug constitutes merely one more antispasmodic that may at times be of use. In those instances where ulcer pain is extremely troublesome *in the night hours*, the *practice* of continuous gastric aspiration during the hours of sleep may give striking relief due to evacuation of the increased volume of nocturnal secretion *that is so characteristic of many* ulcer patients. In particularly intractable pain, the use of constant milk drip administered through an inlying nasal tube occasionally *may be indicated*. *As a routine procedure* however, it seems to have no justification since simpler methods will provide equally satisfactory results.

*In the acute cases* as *therapeutic measures* gradually become effective, it is proper *slowly to increase the interval between* feedings, diminish the number of night feed*ings, and reduce the amount of medication*. Simplification of procedure should be the aim in every instance, and any unnecessary or annoying measures, in the form either of *feedings or of drugs*, should be avoided once symptoms are well under control. A six-meal bland diet and measures directed toward obtaining adequate physical and

mental relaxation are often entirely adequate but careful therapy should be continued until all evidence of ulcer activity has disappeared

The problem of *preventing ulcer recurrences* is a much more difficult one and in many ways presents the chief therapeutic challenge in this disease Although it has been correctly stated that the cause of peptic ulcer is not known there can be no doubt that aggravating factors are well recognized and in many instances can be avoided Dietary regulation must be maintained with frequent simple feedings eaten slowly and on time as a fundamental principle of management This principle must be continuously observed The question of the use of alcohol tobacco coffee and tea becomes somewhat controversial in nature and at times is decided on the basis of emotional factors rather than on satisfactory clinical or experimental evidence The excessive use of coffee tea or caffeine-containing drinks is undoubtedly unwise and should be prohibited inasmuch as these substances stimulate gastric secretion Similarly alcohol is known to produce excessive gastric secretory activity For this reason in almost every instance it should be forbidden In occasional instances as a compromise measure the infrequent use of alcohol just before a main meal may be permitted in order to promote relaxation of the patient More than this should never be allowed The effect of smoking on gastric secretory function is not clear There are unquestionably numerous instances in which excessive smoking seems to promote the continuance of ulcer symptoms and the avoidance of smoking is accompanied by relief Whether the use of tobacco as such is really harmful because of its direct effect upon gastric function or whether it merely reflects increased nervous and emotional tension is a question to which at present there is no definitive answer It is certain from any point of view that excessive smoking should be avoided and in many instances complete avoidance of the use of tobacco is to be desired A point frequently overlooked is the fact that the type of food taken by a given patient is oftentimes of less importance than the regularity with which it is ingested Absolute regularity must be insisted upon as well as frequency and meals should be eaten slowly in a relaxed manner rather than rushed and taken under tension

The factor of emotional stress and strain cannot be adequately evaluated but all the existing evidence points to the fact that prolonged tension particularly tension involving resentment frustration and anxiety may be an important precipitating cause of ulcer recurrence It is therefore of the utmost consequence for the physician to become well acquainted with the problems of individual patients their living habits domestic relations work etc Orthodox psychotherapy is rarely needed although it may occasionally be useful An understanding physicain who has the confidence of his patient may frequently be very effective in preventing the build up of tensions and in helping the patient avoid undesirable situations Unless the patient as well as his ulcer can be managed the therapy of peptic ulcer is almost certain to be unsatisfactory

The factor of intercurrent infection is another variable which may precipitate the recurrence of an ulcer Except for the avoidance of exposure to obvious infective disease no particular measures can be taken to control this threat If however an ulcer patient acquires any intercurrent infection such as influenza common cold sore throat infectious diarrhea and the like it is of the utmost consequence to see that he is immediately placed on intensive ulcer therapy as if an active ulcer were present He should be kept in bed throughout the course of the infection and treated by any or all of the measures previously discussed

One point to emphasize is that many of the newer antibiotics such as aureomycin terramycin and chloromycetin may cause local gastric irritation with nausea and vomiting Such a result is extremely undesirable in an ulcer patient and the use of these drugs should be avoided unless they are absolutely indicated in order to manage an infectious episode Similarly the use of aspirin as a symptomatic measure in the control of arthritic pains or headaches should be avoided in patients with an ulcer history If salicylate therapy is necessary then the use of enteric-coated aspirin tablets is pref

erable in order to avoid gastric irritation. Finally, it should be pointed out that the therapeutic use of the corticosteroids ACTH and cortisone, is absolutely contraindicated in any patient in whom an ulcer is suspected or is known to have previously occurred. These agents stimulate gastric secretion to a very great degree, and numerous instances are already on record in which corticosteroid therapy has been complicated by the recurrence of a peptic ulcer with perforation or hemorrhage.

Careful radiation therapy of the gastric area may constitute a valuable but unpredictable therapeutic measure in otherwise intractable cases.

*Complications.*—The important complications of peptic ulcer are acute perforation, hemorrhage and obstruction.

*Acute perforation* is a frequent complication of peptic ulcer and, unless quickly recognized, is extremely dangerous. The diagnosis of acute perforation is rarely difficult. In most instances the patient is suddenly aware of acute upper abdominal pain which is extremely severe and may be aggravated by motion or by breathing. If there is much leakage through the perforation, fluid and air may spread under one or the other diaphragm with pain radiating typically to the trapezius ridge. As a rule the pain is so intense that the patient holds himself in a very rigid fashion. Palpation of the abdomen reveals boardlike rigidity and respirations are short and rapid. The patient may be cold, and at first, his pulse is not rapid. His temperature may be subnormal. If the condition remains unrecognized and a serious leakage has occurred, the patient's condition rapidly deteriorates with a steadily rising pulse. If operation is not performed, general peritonitis may ensue. Hippocratic facies may be noted, and the patient may die in the course of a few days. The differential diagnosis is usually not difficult, particularly if it is known that the patient has a peptic ulcer. The condition must be differentiated from acute pancreatitis, acute appendicitis, coronary thrombosis, lobar pneumonia, biliary or renal colic, and tabetic crisis. The absence of shock so commonly noted in acute pancreatitis and the boardlike rigidity of the abdomen, together with the suddenness of the onset of symptoms, are the most important diagnostic points. Very occasionally, leakage may occur from a perforated ulcer, with drainage into the pelvis, thus simulating a ruptured ectopic pregnancy or a twisted ovarian cyst. In mesenteric thrombosis and in intestinal obstruction, pain is apt to be peristaltic in nature and abdominal rigidity is much less marked. A film of the abdomen may reveal air under the diaphragm and this constitutes important confirmatory evidence in favor of a perforated ulcer. Films should be taken with the patient in the horizontal and sitting posture if this is possible. Small perforations may occur which may spontaneously seal off. Under such conditions, the patient rarely presents the characteristic picture suggested above.

In almost every instance where the diagnosis is made, surgical interference is indicated and should be carried out as soon as possible. The longer the period of time that elapses between perforation and operation, the poorer the prognosis. Perforation of a peptic ulcer accounts for the vast majority of ulcer deaths, but if operation is performed within 10 or 12 hours of the accident, the survival rate is high. If perforation occurs shortly after a meal, the danger is greater because of the greater spillage of infected contents into the abdominal cavity. The operation of choice is that of closure, and, as a rule, no further procedure should be carried out. Antibiotics should be used in most instances to prevent spreading peritonitis, and in case in which conservative measures seem indicated after proper surgical consultation, antibiotic treatment is definitely indicated. Obviously, the ingestion of food or fluid by mouth should be carefully avoided once the diagnosis is suspected. In certain cases, the patient may not be seen by a doctor in the early stages of the complication, or a correct diagnosis may not have been made for many hours after the event has occurred. If this is the case and a delay of many hours has resulted, then operation is contraindicated for the moment, and the patient should be treated most conservatively, feeding or the giving of any fluids by mouth being forbidden. The patient should be placed in a semi-upright position, kept under continuous morphine administration.

and given adequate doses of penicillin streptomycin or possibly aureomycin by the intravenous route Such measures however are justified only where the diagnosis has been delayed beyond the early stages of the complication In recent years there has been an attempt to treat patients having perforated peptic ulcers without operative interference and good results have been claimed In general however present opinion would seem to indicate that the only proper therapeutic approach to the problem of perforation is early diagnosis and early operative intervention It should be added that successful surgical treatment of an acute perforation of peptic ulcer does not solve the ulcer problem it merely handles the existing emergency Subsequent perforations may occur and the ulcer problem continues unchanged regardless of surgical closure of the perforation

*Chronic perforation* may occur in which a deeply penetrating ulcer breaks through the wall of the stomach and becomes walled off in the body of the pancreas or liver Such an occurrence represents merely the extension of a very active inadequately treated ulcer and does not require immediate surgical treatment Chronic perforation of a jejunal ulcer may result in a gastrojejunocolic fistula a condition which demands elective surgery but does not result in an acute emergency

*Massive hemorrhage* occurs as a serious complication of peptic ulcer in a high percentage of patients It may become evident either by the vomiting of gross blood or by the passage of tarry or bloody stools If bleeding is sufficient in amount and occurs fairly rapidly the stools may contain loose or semi coagulated material resembling currant jelly If bleeding occurs more slowly the material becomes black in color and pitchy in consistency The variation in the character of the stool after massive bleeding from an ulcer depends very definitely upon the two factors noted—speed and quantity As little as 60 cc of blood may produce a tarry stool Massive bleeding may occur with no vomiting whatever Or vomiting may be delayed in which event the vomitus will resemble coffee grounds or may even consist of black rather than reddish or brownish liquid The mortality rate from gross hemorrhage probably is in the vicinity of 3 or 4 per cent of all cases For those over forty five or fifty the mortality rate steadily increases due possibly to the fact that in older people arterial bleeding is less readily controlled Although statistics vary hemorrhage in younger individuals probably carries a risk of about 1 or 2 per cent After the sixth decade the risk may be as high as 10 or 15 per cent These figures however undoubtedly are modified by the adequacy of treatment during the acute episode

The symptoms associated with massive hemorrhage are essentially those of acute blood loss with weakness dizziness headache extreme thirst sweating rapid respirations syncope and collapse The hemorrhage may have been preceded by a period of epigastric pain typical of peptic ulcer but in very many instances pain is lacking and bleeding may occur totally without warning When pain has been present it is commonly noted that discomfort ceases with the onset of bleeding If bleeding continues the pulse rate rises the blood pressure drops and the pulse pressure becomes reduced The patient may go into shock unless bleeding ceases spontaneously or blood is replaced by transfusions The red-cell count the hemoglobin concentration and the hematocrit may remain practically normal for some hours but gradually drop as plasma volume is maintained by dilution In the presence of major hemorrhage there is a rise in the nonprotein nitrogen of the blood which remains elevated as a rule for several days Usually bleeding stops spontaneously but if a large artery has been eroded either the pancreatico-duodenal or the gastric coronary artery hemorrhage may be continuous with a steady increase in associated symptoms of blood loss

The diagnosis of upper gastrointestinal bleeding is usually obvious but in the absence of a known ulcer history it is frequently impossible to determine the source of bleeding immediately Physical examination is of the utmost importance in those instances in which the existence of a peptic ulcer is not known The presence of slight jaundice spider angiomata a spleen that is enlarged to percussion or a palpable liver

erable in order to avoid gastric irritation Finally, it should be pointed out that the therapeutic use of the corticosteroids ACTH and cortisone is absolutely contraindicated *in any patient in whom an ulcer is suspected* or is known to have previously occurred These agents stimulate gastric secretion to a very great degree, and numerous instances are already on record in which corticosteroid therapy has been complicated by the recurrence of a peptic ulcer with perforation or hemorrhage

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cancer and the like if an ulcer is not present The technique of such an examination has already been discussed and requires close coöperation between the radiologist and the physician If massive bleeding from an ulcer does not stop within a reasonable length of time and an adequately trained surgeon is available radical surgery is occasionally indicated as a life-saving procedure Such a decision is at times extremely difficult and operation should not be attempted unless very competent surgical skill is at hand Subtotal resection as an emergency procedure is not desirable in most instances but uninterrupted bleeding for two or three days may make such a decision necessary for in this event the ulcer has eroded into a major vessel and caused a situation that can be handled only by heroic measures With the availability of trained surgeons and an adequate supply of blood such emergency surgery has lost many of its terrors The persistence of bleeding with a fairly rapid *rate of blood loss justifies the administration* of whole blood at a much more rapid rate than that usually employed and at times the blood may have to be given very rapidly in order to carry the patient until proper surgery can be performed

If the episode of major bleeding terminates successfully under medical management consideration of future treatment should then be discussed In many instances elective subtotal gastrectomy should be planned in order to reduce the risk of future hemorrhage There is no unanimity of opinion as to such a decision however and it must always be a matter of individual decision between the physician and the consulting surgeon In older individuals the risk of major bleeding from peptic ulcer is such that surgical intervention at a time when the ulcer is entirely under control would seem to be the safer and more conservative measure In patients who are poor operative risks or in individuals who have never carried out adequate ulcer therapy prior to their hemorrhage conservative medical measures may be proper Such measures should always be accompanied however by a distinct understanding that should subsequent hemorrhages occur subtotal gastrectomy will be performed If elective surgery is performed the patient should understand clearly that this does not entirely preclude the possibility of future hemorrhage and that reasonable regulation of diet and living habits still remains a fundamental consideration

A third complication is that of *pyloric obstruction* Temporary obstruction is frequently encountered as a result of the edema and spasm secondary to an active ulcer in the close proximity of the pylorus Such an occurrence represents a temporary situation which usually responds satisfactorily to good medical management It is not easily differentiated from pyloric obstruction due to cicatricial stenosis at or near the pylorus until the patient has been observed for an appreciable period of time The symptoms of obstruction are common to both situations and consist of epigastric fullness nausea and vomiting Pain may or may not be present but is more likely to be encountered in the presence of an active ulcer In the old cicatrizing lesion pain is a less *prominent feature and gradually increasing* evidence of gastric stasis without pain is the most characteristic symptom Unless the pylorus is completely occluded it is usually found that the vomitus contains bile-stained material which indicates a certain degree of patency The degree of gastric stasis can be most readily determined by gastric aspiration which can and should be carefully measured and recorded together with the amount of vomited material in order to keep an adequate record of daily fluid and electrolyte loss Where minor degrees of stasis are present small frequent feedings should be employed in the manner already described for the treatment of acute peptic ulcer With more complete obstruction such measures may still be utilized but aspiration should be carried out preferably in the morning and in the evening to determine the total amount of stasis On the balance sheet the amount of orally administered fluid should be recorded as well as the amount obtained by aspiration A daily record of intake and output is an absolutely essential measure if proper fluid and electrolyte replacements are to be made It is also essential in order to make a correct and timely decision for operative interference if such is necessary Decision to operate

that is felt by gentle examination, should lead to suspicion of bleeding from esophageal varices rather than from an ulcer, although the two conditions may be coexistent. A visible abdominal mass, other than the liver, should, *of course, suggest the possibility* of gastric cancer, but major bleeding from cancer of the stomach is relatively uncommon. Cautious physical examination may yield no information, and vigorous manipulation and palpation should be avoided. If physical signs other than those associated with active bleeding are not present, the most logical explanation is that of bleeding from a peptic ulcer, inasmuch as this is by far the most common cause of upper gastrointestinal hemorrhage. Further diagnostic measures should be postponed until it is certain that the bleeding has stopped or that the patient is not in shock.

The immediate treatment that is indicated is that of bed rest, elevation of the foot of the bed, and sedation. The administration of morphine to relieve restlessness is the traditional therapeutic measure. In the opinion of the author, the use of morphine is contraindicated, inasmuch as it may produce nausea and vomiting and may cause associated duodenal spasm. Probably a wiser procedure is to administer sodium phenobarbital subcutaneously and to procure further sedation by its periodic use as indicated. At the same time preparation should be made to replace blood loss by whole blood transfusion. If the patient is in shock and blood is not immediately available, solutions of glucose and saline may be given by slow intravenous drip, or plasma may be used. The use of whole blood is preferable, however, and wherever massive hemorrhage has occurred it is probably good judgment to transfuse slowly until it is perfectly certain that there is no danger of shock. From that point on, the use of blood transfusions should be regulated by the level of hematocrit or the hemoglobin level as determined at fairly frequent intervals. Except in rare instances, the blood should be given at a very slow rate. Exceptions to this are rare and will be noted subsequently. In most instances small careful feedings of bland protein-containing food should be administered, once vomiting has ceased. These feedings may be given at half hourly or hourly intervals in amounts ranging from 30 to 60 cc. of milk, or if desired they may be given by constant milk drip; the latter is rarely needed. The program of feeding outlined by Meulengracht in bleeding cases embodies the same principle but permits the use of a variety of foods. As a rule, in the early stages of feeding after hemorrhage it would seem wise, however, to limit the diet to small quantities of food such as whole milk, milk, and lime water or gelatine, as originally suggested by Andresen. The use of amino acids, as suggested by Co Tui, has certain theoretical advantages, but the distaste that most patients have for amino acid preparations is such that ordinarily other types of feeding are more easily tolerated and just as valuable in neutralizing gastric acidity and in providing calories and protein. If vomiting continues, temporary avoidance of oral feeding may be necessary, but this is usually not the case. Constant observation of pulse, blood pressure, pulse pressure, and the general appearance of the patient is of fundamental importance, and evidences of recurrent bleeding or incipient shock should be quickly noted and treated by further careful transfusions. During the early phases of treatment the use of antacids is probably not necessary in the presence of adequate oral feedings. Once the situation seems to be under control, the addition of antacid preparations may be desirable. The replacement of blood by transfusion should be sufficient in amount to maintain the patient well above shock level but should not aim at raising the hemoglobin to high levels. In general, it will be found that it is desirable to maintain a somewhat higher level of hemoglobin in older individuals than is necessary for the younger age group. Once it is certain that bleeding has stopped, therapeutic measures should be carried out as they would be during the course of acute ulcer therapy. If the source of bleeding is not clear, it is important to recognize the wisdom of careful *x*-ray studies just as soon as hemorrhage has ceased. It is extremely important to obtain precise information, if possible, as to the location of the lesion if it is an ulcer, or to demonstrate the existence of other causes, such as esophageal varices

or adjacent jejunum are relatively common. The demonstration of a stomal or jejunal ulcer after posterior gastrojejunostomy may have as high an incidence as 25 per cent or more. Stomal or jejunal ulcer may occur after subtotal gastrectomy, but it is relatively uncommon. The incidence probably is below 5 per cent. When it does occur, the question should be immediately raised whether the resection was adequate—particularly whether the entire pyloric antrum was removed. Failure to accomplish the latter results in stomal ulceration in a very high percentage of cases, and subsequent removal of the remaining pyloric antrum almost invariably controls the situation. Otherwise the problem of stomal or jejunal ulcer presents a very difficult therapeutic problem. At times further radical resection of the stomach is in order. Another maneuver frequently accompanied by a reasonable degree of success is that of vagal section.

A complication of jejunal ulcer is that of gastrojejunocolic fistula, and this invariably requires extremely radical surgery. Such a complication may be encountered in between 5 and 10 per cent of patients with stomal or jejunal ulcers.

In recent years the performance of bilateral vagal section, with or without associated gastrojejunostomy, has been carefully studied by various surgeons and physicians. Vagotomy, when adequately performed, undoubtedly results in a complete inhibition of psychic gastric secretion, in marked reduction of gastric motility, and in the control of otherwise uncomplicated ulcer symptoms. When performed as a single procedure, experience has shown that ulcer recurrences may be expected in an appreciable number of instances. It is therefore not definitive surgery. If combined with a posterior gastroenterostomy, the results may be much more successful, and enthusiasm for this procedure is properly based upon the experiences of Dragstedt and Palmer. It is fair to comment, however, that more years must elapse before the procedure can be properly evaluated. The ultimate value of such a combined operation will depend upon its ability to control symptoms over a period of many years without ulcer recurrence. It has the theoretical advantage that it leaves the patient with an intact stomach, and in the absence of obstruction permits a reasonable amount of food to proceed through the pylorus into the duodenum with the accompanying physiological stimulation of duodenal and pancreatic secretions.

*Complications of Surgery.*—Any discussion of ulcer surgery should include two considerations aside from the immediate risk of operation and the subsequent possibility of stomal or jejunal ulcer. One possible complication is the so-called *dumping syndrome*. Symptoms of this syndrome may occur either after subtotal gastrectomy or after simple gastrojejunostomy. In the first weeks after operation it is not at all uncommon to encounter this particular set of symptoms, but in the vast majority of cases adjustment takes place so that it does not constitute a major problem in later months. In from 10 to 15 per cent of individuals who have either a subtotal gastrectomy or a gastrojejunostomy, troublesome symptoms are encountered which appear either a few minutes after the intake of food or after a delay of from two to four hours. In all but a few cases symptoms occur shortly after eating—epigastric fullness, discomfort, occasionally pain, accompanied by a feeling of weakness or giddiness, excessive sweating and tachycardia or bradycardia, with alterations in blood pressure, either elevation or reduction. In rare instances, actual syncope may occur. Although suggestive of a hypoglycemic attack, a reduction in the blood sugar is not present, and the symptoms in all probability are the result of an active overfilling of the proximal jejunum and a violent vasomotor disturbance secondary to autonomic nervous stimulation. Relief is usually obtained by lying in a horizontal position for a few minutes, though sometimes resting thus for half an hour or more may be required. The symptoms may be relatively mild or they may be so intense that the patient may fear the act of eating to a degree which precludes adequate nutrition. The nature of the ingested food is of some importance but does not determine the appearance of symptoms. Sugary or highly sweetened foods seem to provide one factor in the production of attacks. In some individuals the use of milk seems to be a pre

should depend upon the continuance of obvious obstruction while the patient is under close observation. If an adequate caloric intake with sufficient fluid cannot be given by mouth within a reasonable length of time surgery is mandatory. If however, evidence of gastric stasis diminishes daily, conservative medical measures should be continued, with the expectation that satisfactory control of the immediate situation will be obtained on the subsidence of the active ulcer. Where there has been prolonged excessive vomiting before admission to the hospital chemical determinations of serum electrolytes are frequently indicated in order to plan for the proper administration of sodium chloride, and potassium ions. In addition, it is important to attempt to meet caloric needs by proper parenteral administration of glucose or glucose and amino acids, in solution. This is particularly true if the situation seems to be approaching a decision for surgical intervention inasmuch as the depleted patient may tolerate surgery very poorly. It is obvious that estimates of the obstructing lesion should be confirmed by careful radiological study but it should be pointed out that such studies are of little value unless the stomach is completely emptied by previous aspiration before a barium meal is taken. In the case of pyloric obstruction secondary to an acute ulcer with little or no cicatricial stenosis the use of atropine and sedation may be the most important therapeutic measure other than routine careful feeding. Conversely where cicatricial stenosis of major degree is encountered and there is marked dilatation of the stomach from long standing stenosis atropine or other antispasmodics are probably contraindicated. As already noted marked cicatricial stenosis is in itself an indication for operative interference and if the patient can be properly called a good operative risk subtotal gastrectomy is the operation of choice. Occasionally posterior gastrojejunostomy may be the desirable procedure. In patients having repeated attacks of pyloric obstruction secondary to ulcer recurrences, surgery may eventually be necessary, either because of progressive stenosis secondary to healing or because of continued failure to control the ulcer situation to a degree where the patient can lead a useful life.

Perforation and hemorrhage may coëxist and such a complication presents an extremely difficult problem. The indications for surgery are clear as soon as the diagnosis of perforation is established. The treatment of bleeding will of necessity depend upon findings at operation but in any event replacement of blood in adequate amounts is absolutely essential.

*Intractability.*—One final complication of peptic ulcer that requires consideration of surgery must be briefly mentioned—namely, "intractability." Such a term is necessarily vague and difficult of definition. Frequently intractability suggests that medical management by the physician has been totally inadequate. In many instances, it implies a lack of understanding of the fundamental principles of ulcer management both by the physician and by the patient. In other cases however intractability may imply failure of adequate medical therapy to control ulcer symptoms in such a way as to permit the patient to carry on a normal existence. Under these circumstances ulcer surgery is certainly indicated. In still other instances, intractability may be due to the fact that the patient is essentially a neurotic individual in which case either medical or surgical treatment may fail completely to control not only the ulcer symptoms but other complaints characteristic of the neurosis. In this combination of a neurotic patient and chronic peptic ulcer surgery is usually contraindicated because the patient will not be rendered a useful and relatively symptom free individual. Psychotherapy is the only approach to the problem and even this is often entirely unsuccessful.

*Surgical Treatment.*—The surgical treatment of peptic ulcer has already been alluded to. As on other aspects of the ulcer problem complete unanimity of opinion does not exist but the view of most experienced clinicians suggests that subtotal gastrectomy is at present the operation of choice if a competent sugeon is available and the proper indications exist. The procedure of posterior gastroenterostomy is usually ill advised inasmuch as ulcer recurrences at the original site or more frequently in the stoma

or adjacent jejunum are relatively common The demonstration of a stomal or jejunal ulcer after posterior gastrojejunostomy may have as high an incidence as 25 per cent or more Stomal or jejunal ulcer may occur after subtotal gastrectomy but it is relatively uncommon The incidence probably is below 5 per cent When it does occur the question should be immediately raised whether the resection was adequate—particularly whether the entire pyloric antrum was removed Failure to accomplish the latter results in stomal ulceration in a very high percentage of cases and subsequent removal of the remaining pyloric antrum almost invariably controls the situation Otherwise the problem of stomal or jejunal ulcer presents a very difficult therapeutic problem At times further radical resection of the stomach is in order Another maneuver frequently accompanied by a reasonable degree of success is that of vagal section

A complication of jejunal ulcer is that of gastrojejunocolic fistula and this invariably requires extremely radical surgery Such a complication may be encountered in between 5 and 10 per cent of patients with stomal or jejunal ulcers

In recent years the performance of bilateral vagal section with or without associated gastrojejunostomy has been carefully studied by various surgeons and physicians Vagotomy when adequately performed undoubtedly results in a complete inhibition of psychic gastric secretion in marked reduction of gastric motility and in the control of otherwise uncomplicated ulcer symptoms When performed as a single procedure experience has shown that ulcer recurrences may be expected in an appreciable number of instances It is therefore not definitive surgery If combined with a posterior gastroenterostomy the results may be much more successful and enthusiasm for this procedure is properly based upon the experiences of Dragstedt and Palmer It is fair to comment however that more years must elapse before the procedure can be properly evaluated The ultimate value of such a one based operation will depend upon its ability to control the symptoms over a period of [illegible] years without ulcer recurrence It has the theoretical advantage that it leaves the patient with an intact stomach and in the absence of obstruction permits a reasonable amount of food to proceed through the pylorus into the duodenum with the accompanying physiological stimulation of duodenal and pancreatic secretions

*Complications of Surgery* —Any discussion of ulcer surgery should include two considerations aside from the immediate risk of operation and the subsequent possibility of stomal or jejunal ulcer One possible complication is the so-called *dumping syndrome* Symptoms of this syndrome may occur either after subtotal gastrectomy or after simple gastrojejunostomy In the first weeks after operation it is not at all uncommon to encounter this particular set of symptoms but in the vast majority of cases adjustment takes place so that it does not constitute a major problem in later months In from 10 to 15 per cent of individuals who have either a subtotal gastrectomy or a gastrojejunostomy troublesome symptoms are encountered which appear either a few minutes after the intake of food or after a delay of from two to four hours In all but a few cases symptoms occur shortly after eating—epigastric fullness discomfort occasionally pain accompanied by a feeling of weakness or giddiness excessive sweating and tachycardia or bradycardia with alterations in blood pressure either elevation or reduction In rare instances actual syncope may occur Although suggestive of a hypoglycemic attack a reduction in the blood sugar is not present and the symptoms in all probability are the result of an active overfilling of the proximal jejunum and a violent vasomotor disturbance secondary to autonomic nervous stimulation Relief is usually obtained by lying in a horizontal position for a few minutes though sometimes resting thus for half an hour or more may be required The symptoms may be relatively mild or they may be so intense that the patient may fear the act of eating to a degree which precludes adequate nutrition The nature of the ingested food is of some importance but does not determine the appearance of symptoms Sugars or highly sweetened foods seem to provide one factor in the production of attacks In some individuals the use of milk seems to be a pre-

cipitating factor, although the symptoms are in no way suggestive of an allergic response. The *volume of the meal* may be important, and in most instances where symptoms are at all prominent, frequent feedings of small amounts may be helpful. Atropine or banthine taken in adequate doses fifteen or more minutes before the intake of food may prevent attacks or minimize their severity. In a few instances, the symptoms are so extreme that they result in a totally inadequate food intake with an accompanying severe malnutrition. At times they are *essentially very intractable*. They tend to occur in the more reactive rather neurotic individuals. The dumping symptoms which occur several hours after the intake of food are relatively uncommon and may be a reflection of a lowered blood sugar. This is not always the case, as *proved by chemical determinations of the level of sugar in the blood* but symptoms are not infrequently benefited by the immediate administration of food. As a rule they are much less severe and less incapacitating than those symptoms already described.

A second complication of subtotal gastrectomy is that of *inadequate food absorption* and consequent malnutrition which may be quite independent of dumping symptoms. It has been shown by various investigators *that patients with this complication tend to* lose excessive amounts of fat and slightly excessive amounts of nitrogen in the stools. Such is invariably the case in the first few days or weeks after the operation but adjustment usually takes place without difficulty. The explanation of this phenomenon is not clear. To date, it has not been shown to be due to inadequate pancreatic digestion or to any other known factor. It is possible that it is dependent upon the removal of the lower portion of the stomach which may produce a secretion capable of affecting the physiological absorption of lipoids and to a lesser extent other substances. Therapeutic measures so far have been *quite ineffective in* controlling this particular complication which is serious because it results in chronic undernutrition. The oral use of certain detergents, such as 'Tween 80,' to improve the emulsification of fat has, in some instances, been helpful in improving fat absorption. In most instances, the most important therapeutic measure consists in the administration of excessive amounts of food. Such a measure is difficult and is not easily tolerated by most patients. It is essential, however, if the wastage of calorific material is to be covered to a sufficient degree to permit maintenance of weight or gain in weight. In order to accomplish this, diets *high in concentrated foods* and relatively low in total bulk must be administered.

BENIGN GASTRIC ULCER VERSUS GASTRIC CARCINOMA.—Up to the present point, *gastric ulcer has been discussed in the same* category as duodenal ulcer. Additional consideration, however, must be given to the fact that benign gastric ulcer and carcinoma of the stomach may be readily confused. The controversy as to the possible degeneration of a benign ulcer into a car*cinomatous lesion has not been settled and* is for practical purposes purely academic. The important consideration is that the demonstration of an ulcerating lesion of the stomach imposes the obligation of ruling out the probability of gastric cancer before final therapeutic decisions can be made. Furthermore, no physician has a right to accept the responsibility of conservative medical care of a proved gastric ulcer unless he is fully prepared to follow the patient's course for an *indefinite time with periodic checkups*. Differentiation between a benign and malignant lesion of the stomach in doubtful cases is never definitive. In obvious cancer of the stomach the radiological findings are clear cut, and there need be no hesitation in making the diagnosis. The real problem is encountered where an ulcerating lesion appears to be benign and therefore should be treated conservatively if possible. Clinical experience shows that malignant lesions occur as a rule in the later decades whereas benign ulcer most commonly appears in the earlier decades of life. Typically the history of gastric cancer is relatively short, that of a benign lesion as a rule covers a period of years. Neither fact is in any way conclusive in making individual diagnoses. On physical examination the finding of an epigastric mass may, *on rare occasions*, be associated with a benign lesion but this fact should never be accepted as a justification for con

servative measures The finding of a palpable tumor in relation to an ulcerating lesion of the stomach or pylorus should always lead to a decision in favor of radical gastric surgery Gastric analysis in carcinoma of the stomach may reveal normal or relatively normal gastric secretion Therefore the finding of normal acid values does not preclude the possible presence of malignancy On the other hand achlorhydria after histamine stimulation in a patient with a demonstrated gastric lesion should always be taken as presumptive evidence of cancer Cytological studies of gastric contents by well trained observers may be of real help but negative findings offer no assurance that the lesion is benign Positive findings are diagnostic Radiological examination of the stomach may suggest a benign lesion because of the location of the ulcer and the absence of rigidity and of interruption to normal peristaltic waves Most benign lesions are found in the middle of the lesser curvature The majority of malignant lesions are encountered in the region of the antrum All these criteria are of relative value however and cannot give complete assurance as to the nature of the process Gastroscopic observations may show the clean punched-out ulcer characteristic of a benign lesion or one with the irregular partially undermined edges and dirty base typical of malignancy An ulcer of apparently benign appearance however may contain early malignant changes which cannot be determined by gastroscopic observation Additional evidence may be obtained by biopsy through the operating gastroscope but only positive findings are definitive In spite of the fact that an absolute diagnosis of a benign lesion is not possible it is probably unwise and unnecessary to adopt the radical attitude that every gastric ulceration requires radical resection If the physician is prepared to follow the patient carefully it is frequently proper to elect a course of watchful waiting In a patient with a gastric ulcer who has a typical ulcer history a normal amount of free acid a negative cytological study and a satisfactory gastroscopic examination confirming the benign appearance of the lesion routine medical ulcer therapy may be instituted This should be done with the understanding that careful x ray and/or gastroscopic checkups will be performed at regular intervals Evidence of healing should be obtained by x ray examination at an interval of no longer than one month after the institution of medical treatment If progress is apparently satisfactory and the size of the crater has appreciably diminished then a second x ray or gastroscopic examination should be performed at the end of another three or four weeks If at this time the ulcer crater has disappeared and symptoms are completely under control then it may be proper to continue further medical management Checkup examinations should be made periodically at intervals of several months or at any time that symptoms recur It should never be forgotten that apparently complete healing may occur in a small ulcerated cancer The mucosa may bridge the area of malignant involvement so that all evidence of ulceration has disappeared Fortunately such an occurrence is rare Failure to show evidence of healing in a reasonable length of time or failure to control symptoms that recur should require a review of the entire situation and in many instances surgical intervention should be chosen as the proper therapeutic move This is particularly true where gastric ulceration is demonstrated in the region of the pyloric antrum or the prepyloric area Ulcers along the greater curvature of the stomach or in unusual areas other than the mid lesser curvature should always be viewed with extreme suspicion It is better occasionally to resect a benign lesion that to miss an early diagnosis and forfeit the opportunity for a successful cure of gastric cancer

Cancer of the first portion of the duodenum is so rare that consideration of this possibility need not be seriously entertained except in cases in which the x ray findings are very abnormal or the lesion and the patient s symptoms are unusually intractable

Gastric Tumors —Gastric tumors include those of epithelial origin such as adenomas papillomas adenomatous polyps and adenocarcinomas and also the less common tumors of mesenchymal origin The latter include tumors classified as fibromas

myomas leiomyomas, sarcomas, dermatoid cysts hemangiomas, lipomas and the various forms of lymphomatous tumors The symptoms of gastric tumor are in no way diagnostic They vary according to the complications arising from the tumor itself such as ulceration bleeding or the development of the tumor to a size sufficient to cause obstruction Thus the presence of a leiomyosarcoma may be first suspected when the patient develops symptoms of ulceration with or without bleeding Adenomatous polyps for example may present frank gastric bleeding is the initial symptom Symptoms directly due to the tumor may be entirely absent but minor bleeding may occur with resulting anemia which necessitates a search for the source of the hemorrhage The diagnosis of tumor in the absence of a visible or palpable mass in the epigastrium will be entirely dependent upon radiological or gastroscopic studies Gastric polyps may be benign or malignant but once demonstrated should usually be treated by surgical removal inasmuch as the probability of malignancy or of malignant degeneration exceeds the risk of surgery In pernicious anemia and in atrophic gastritis polyps are occasionally encountered Bleeding with resulting anemia is the usual clinical finding and such polypi should always be resected, either by local removal or by subtotal gastrectomy



Fig 201 —Adenomatous polyp of the stomach adjacent to a fungating carcinoma (Herbut s Surgical Pathology)

*Adenocarcinoma* of the stomach is extremely common and early diagnoses are still too infrequent with the result that the mortality rate associated with this condition is extremely high Gastric cancer is probably responsible for a greater number of deaths than any other form of cancer The etiology is unknown but heredity may play an important role It is rarely encountered until the third decade and is most commonly found after the age of thirty five Symptomatically gastric cancer may be silent until it is far advanced As already indicated even when symptoms are present the history is relatively short and may frequently be measured in weeks or a few months When symptoms are present they usually are characterized by loss of appetite and diminished food intake with loss of weight and relatively mild epigastric distress It is important to point out that one of the most

common symptoms is that of gradually increasing constipation without any obvious cause At times the story may mimic that of peptic ulcer, but this is the exception rather than the rule, inasmuch as pain may occur during the meal and frequently is not relieved either by the intake of food or by the use of antacids Nausea and vomiting are not uncommon and are not necessarily associated with definite obstruction The vomitus may contain blood and hematemesis or tarry stools may be early clinical manifestations of the disease Massive bleeding is not particularly common although continuous oozing is rather characteristic with a resulting severe anemia As a rule the anemia is that associated with blood loss but occasionally macrocytic anemias are encountered Perforation may occur but is relatively uncommon Physical examination is all too frequently noncontributory except for evidences of anemia and loss of weight A palpable mass may be encountered and it is important to search for evidences of hepatic enlargement the existence of a Virchow node or metastatic lesions in the ovaries or on the rectal shelf Except for cytological studies of the gastric contents laboratory examinations yield no definite diagnostic information Gastric achlorhydria is common but as already noted normal secretory findings are present in an appreciable number of instances The presence of blood in the gastric contents or in the stools merely demonstrates the existence of an ulcerating or erosive lesion and the degree of anemia indicates the severity of the underlying condition Definite diagnosis must be established by careful roentgenological studies and in dubious cases by thorough examination of the stomach by gastroscopy Once the diagnosis is established or is presumed to be probable radical surgery is indicated The only contraindications to such a maneuver are obvious and advanced metastases or evidence that the patient is a poor operative risk either because of the advanced state of the disease or because of associated conditions Where obstruction to the outlet of the stomach is present gastroenterostomy is a justifiable procedure as a palliative measure Radiation therapy to date has not proved to be of therapeutic value The prognosis of adenocarcinoma of the stomach depends upon two factors The first and of fundamental importance is that of early diagnosis In addition the type of carcinoma as classified pathologically may give a reasonable clue as to the speed of growth and therefore the



Fig 202 —Diffusely spreading carcinoma involving the pyloric portion of the stomach (Herbut s Surgical Pathology )

probability of metastasis In favorable cases, where "doubtful" lesions have been removed surgically long survival rates and apparent cures may be reasonably expected The total number of such satisfactory results is still relatively small Easily diagnosed carcinoma of the stomach has a much poorer prognosis but this fact should not militate against radical surgical procedures

*Scirrhous carcinoma* is characterized by diffuse infiltration and thickening of the wall of the entire stomach, without discrete, easily identified ulceration This type is particularly difficult of diagnosis because it is frequently asymptomatic and may be missed even with careful x ray studies At times it is confused with advanced hyper trophic gastritis

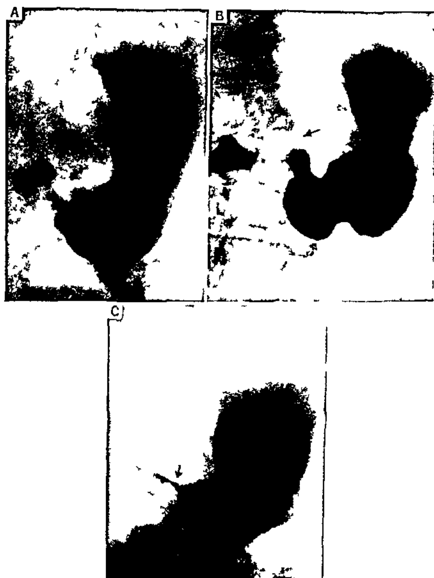



Fig 203 —Roentgenograms showing A spasm of the prepyloric antrum with no organic lesion B early malignant lesion of the prepyloric antrum C late malignant lesion of the prepyloric antrum (Portis Diseases of the Digestive System )

The *tumors of mesenchymal origin* have no distinct clinical characteristics and their detection depends upon the use of the measures outlined above Radiologic examination may indicate clearly that deforming lesions of the stomach are present but ap-

parently arise beneath the mucous membrane thus indicating the source of the growth Ulceration may occur however and the appearance of any of these tumors may be difficult to differentiate from that of carcinoma Occasionally diagnosis may be determined by examination of biopsy material obtained through an operating gastroscope but in most instances a final diagnosis is made only at the time of operation which is always indicated as the proper therapeutic measure

Special reference should be made to the relatively uncommon involvement of the stomach by *lymphoma of the Hodgkin s type* Although rare this disease may involve only the stomach It is characterized by a diffuse infiltration of the major part of the organ The radiological and gastroscopic findings are strongly suggestive of hypertrophic gastritis of an extreme degree with marked distortion of gastric rugae Diagnosis may be made by biopsy material obtained at gastroscopy Symptoms are usually those of an intractable gastritis and when radiologic or gastroscopic findings are difficult to interpret surgical exploration is indicated to obtain adequate biopsy material Identification of the lesion by histological study is important inasmuch as very satisfactory results may be obtained either by total gastrectomy or at times by careful roentgen ray therapy of the stomach itself provided the disease has not involved other areas in the body

# DISEASES OF THE SMALL INTESTINE

Small bowel disturbances may be associated with developmental abnormalities tumors mechanical block by foreign bodies or by torsion intussusception inflammatory or infiltrative diseases or specific infections

## INTESTINAL OBSTRUCTION

With the exception of diffuse inflammatory disease of the small intestine symptoms related to jejunal and ileal abnormalities are essentially those of varying degrees of intestinal obstruction These symptoms consist of crampy peristaltic pain usually localized in the periumbilical area regardless of the level of the disease process In conditions affecting the terminal ileum the symptoms may be referred to the right lower quadrant When there is more than slight obstruction to the passage of intestinal contents at a given point pain is usually accompanied by nausea and vomiting distention high pitched peristaltic sounds that are obviously increased in frequency and intensity above normal and, occasionally local tenderness The greater the degree of obstruction the greater will be the magnitude of symptoms and dehydration and electrolyte loss will be pronounced as a result of prolonged vomiting The vomitus has a fecal odor Films of the abdomen characteristically reveal dilated loops of the small bowel proximal to the obstructed area and these loops frequently show fluid levels

DEVELOPMENTAL ABNORMALITIES consist essentially of diverticula which may be encountered at any level They are rarely the cause of symptoms and when demonstrated accidentally during the course of radiological examination they should be noted and then disregarded unless there is evidence of stasis or bleeding that can be explained in no other fashion

*Meckel s Diverticulum* —One exception to the above rule is the condition known as Meckel s diverticulum This diverticulum is a rather common finding which represents a remnant of the omphalomesenteric duct and is to be found in the ileum at a point approximately 60 to 80 cm above the ileocecal valve Meckel s diverticula frequently contain islands of gastric mucosa and accordingly are associated with the occurrence of ulceration in the ileum opposite or adjacent to the stoma of the pouch In children or young adults this may provide a source of periumbilical pain and bleeding If pain is sufficiently marked it may suggest partial obstruction because of its peristaltic nature Actually partial obstruction may occur due to a local inflammatory process, with swelling and cicatrization Volvulus intussusception and strangulation may also occur and the clinical picture may be that of an acute abdominal emergency It is extremely

rare for the radiologist to be able to demonstrate either the diverticulum or the area of ileum involved unless there is frank obstruction. At times the only finding of importance may be that of anemia, due to blood loss, and careful search may reveal occult blood in the stools. At other times bleeding may be brisk and black or reddish stools may occur in the attacks usually with pain. The condition should always be considered in the presence of otherwise unexplained bleeding from the gastrointestinal tract in younger individuals. The only *treatment is that of surgical resection*.

FOREIGN BODIES may cause local obstruction at any level but the usual site is at or near the ileocecal valve. This obstruction may be due to objects that have been swallowed and have passed the pylorus. One particular form of intestinal obstruction secondary to a foreign body is that caused by a single large gallstone which has perforated through the wall of the gall bladder and has developed a fistulous opening into the duodenum and thence passed into the small intestine. Physical examination may reveal only distention and rather high pitched peristalsis characteristic of obstruction. There may be however a point of local tenderness over the obstructed area which is usually to be found in the right lower quadrant. Roentgenological examination may reveal the presence of a foreign body. Fever and leukocytosis may be present and serious dehydration and loss of electrolytes may occur as a result of persistent vomiting. The condition represents a surgical emergency, and no other form of treatment should be considered. In the case of a gallstone ileus, diagnostic help may be obtained if the history can bring out the fact that the patient has previously suffered from attacks of biliary colic.

VOLVULUS OR INTUSSUSCEPTION.—In addition to obstruction caused by foreign bodies, similar symptoms may occur as a result of volvulus or intussusception. At times, kinking or torsion may be produced without any obvious cause. They may be due, however, to the scars of previous surgery, such as adhesions from a previous appendectomy or from other forms of abdominal surgery. They may also be associated with pelvic disease, causing kinks or torsion of loops of ileum secondary to endometrial implants, carcinoma of the uterus or ovaries, or heavy radiation of the pelvis for malignant disease. A careful history may bring out a record of previous therapeutic measures which may have led to the existing situation.

Intussusception is the invagination of one portion of the intestine into an adjacent segment. In almost every instance, it occurs from above downward. It is most frequently encountered in infants and children. *Precipitating causes include tumors of* all sorts, foreign bodies and Meckel's diverticula, as noted above, and focal areas of inflammatory disease. That portion of the gut which is invaginated into another segment becomes edematous and hyperemic with resulting secretion of excessive amounts of mucus, gross bleeding and, if untreated, necrosis and gangrene.

A further common cause of intestinal obstruction is that associated with inguinal or femoral hernia. Under such circumstances obstructive symptoms may be associated with invagination of a loop or bowel in the hernial sac with kinking, occlusion and possibly with strangulation.

*Treatment*.—In all the situations cited above intestinal obstruction is the presenting difficulty and in most instances surgical intervention is the treatment of choice. If distention is marked, decompression by means of intestinal intubation is of extreme importance as a preliminary measure except where strangulation of the bowel is suspected; in that case immediate surgery is indicated. If decompression is carried out *special attention must be paid to replacement* of fluid and electrolytes which will have been lost by the decompression technique or by previous vomiting. Replacement must be carefully carried out before and after surgery. The exact details of the surgical procedure will depend upon the condition presenting in the abdomen. They may be limited solely to the release of the kinking or torsion, or extreme measures may be required involving resection of areas of gangrenous bowel in advanced cases. Intensive antibiotic treatment may be necessary in individual instances. For the ob

structive symptoms of abdominal pain nausea and vomiting morphine is the drug of choice

## SMALL-BOWEL TUMORS

Small bowel tumors are relatively uncommon They are encountered with much less frequency than are tumors in the stomach or in the colon The *diagnosis* of tumors of the small bowel is made on the basis of symptoms of intestinal obstruction or because of evidences of gastrointestinal tract bleeding Localization of these tumors may be accomplished only by careful radiological studies of the small intestine This is a relatively simple matter as far as the duodenum is concerned When the tumors are located in the jejunum or ileum demonstration of one or more tumors may be extremely difficult and will depend upon the skill of the roentgenologist and the fact that in many instances there is partial occlusion of the lumen of the bowel Where symptoms of obstruction are prominent barium studies may be contraindicated because of the risk of increasing the degree of obstruction but under these circumstances abdominal films may show dilated loops above an area of narrowing If obstructive symptoms are not severe then barium given by mouth may be carefully followed by serial examinations throughout the entire length of the small bowel In a high percentage of cases localization of the lesion causing symptoms may be satisfactorily determined Occasionally tumors may be demonstrated by the passage of a double lumen tube with a balloon attached to one lumen Once the tip of the tube is in the small bowel the balloon may be moderately distended and the tube allowed to pass as far as possible Using this technique it is frequently found that the balloon stops at the partially obstructed area which can then be outlined satisfactorily by introducing barium through the open lumen of the second tube

Benign Tumors —The most common benign tumor of the small bowel is *adenoma* which may exist as a single polypoid tumor or there may be multiple adenomata If pedunculated it may cause intussusception The chief consideration in the treatment of adenomatous polyps aside from that of obstruction, is the potential danger of malignancy *Lipomata* are usually single tend to be pedunculated and are chiefly of importance because of the danger from obstruction or bleeding Other benign tumors are classified as *fibromas hemangiomas myelomas* and *chylangiomas* These are of extreme rarity In the duodenum and upper jejunum small nodular masses of aberrant pancreatic tissue may be found which rarely obstruct but may become ulcerated and produce bleeding Rarely, cysts may occur in the small bowel as a result of congenital malformation

Malignant Tumors —Malignant tumors of the small intestine are relatively uncommon but with improvement in radiologic technique they are being more frequently recognized than formerly Symptoms due to adenocarcinoma sarcoma or carcinoids are no different from those caused by any other partially obstructing or ulcerated and bleeding lesion of the small bowel Of these three tumors *adenocarcinoma* is the most common It occurs most frequently in the mid-duodenum but may be found at any level of the small intestine It may occur as a stenosing annular lesion as an ulcerating infiltrating tumor or in the form of a polyp *Sarcoma* is less frequent and pathologically may be classified as lymphosarcoma the commonest or as leiomyosarcoma fibrosarcoma or neurofibrosarcoma Such tumors as a rule are infiltrating in nature but may ulcerate and may produce obstruction *Carcinoid tumors* (argentaffin tumors) are nearly always found in the appendix or in the region of the ileocecum They are derived from the chromaffin system Although usually benign they may show malignant characteristics with steady growth and with metastases They are usually symptomless unless they are very large or occlude the appendix in such a way as to produce symptoms of appendiceal irritation The adenocarcinomata and the sarcomata have a very poor prognosis because they are relatively asymptomatic for a long time with the result that metastases are frequent If recognized surgical intervention is the only form of therapy to be considered

In general it can be said that in the absence of other symptoms the finding of

anemia with occult blood in the stools always warrants a careful search by radiological studies of the entire small bowel in the hope that a localized tumor may be demonstrated and successfully removed

## INFLAMMATORY DISEASE OF THE SMALL INTESTINE

Inflammatory disease of the small intestine may be due to specific infectious agents such as typhoid or Salmonella infections food poisoning due to specific strains of staphylococci tuberculosis, or to a nonspecific granulomatous process known as regional enteritis Typhoid fever Salmonella infections and staphylococcal food poisoning are discussed elsewhere

*Acute infectious diarrhea* due to infectious agents usually occurs without identification of precise etiology The onset is characterized by anorexia or nausea and vomiting and periumbilical cramplike pains with obvious increase in peristaltic activity and diarrhea Fever may or may not be present At times classified as intestinal grippe at other times designated as food poisoning these episodes are usually short lived, lasting only a few days The onset is abrupt and abdominal pain may be rather severe requiring medication Without marked elevation of temperature or severe prostration and without any history of preceding attacks infectious diarrhea is best treated with immediate rest in bed frequent small feedings of very bland food and avoidance of more than moderate amounts of fruit juice and articles of food containing a large amount of residue Iced drinks should be avoided Fluids should be taken if tolerated preferably in the form of clear hot drinks of broth If there is any real reason to suspect contaminated food as a precipitating cause early purgation with castor oil may be desirable If diarrhea has persisted for many hours or for several days such a measure is to be avoided The use of simple bismuth preparations with or without opium, in the form of paregoric or tincture of opium, may quite adequately control abdominal discomfort and excessive bowel activity Unless there is a striking elevation of temperature, it will be wise to avoid the use of the newer antibiotics such as aureomycin and terramycin inasmuch as these may aggravate the diarrhea and nausea and may in themselves prolong the irritation of the bowel even to the extent of causing bleeding from the lower intestinal tract If the condition comes rapidly under control then a normal diet may be gradually resumed, but it should be remembered that such an infectious episode leaves the entire intestinal tract in a rather irritable condition and failure to avoid excessive roughage may cause a renewal of symptoms If diarrhea persists over any extended period—particularly if there is an associated elevation of temperature then search should be made for specific infectious agents More extensive studies may be indicated It should be particularly emphasized that in infants small children and depleted older people attacks of infectious diarrhea may be very serious due to rapid depletion of fluids and electrolytes Under these circumstances adequate replacement therapy must be provided and failure to do so may occasionally result in a fatal outcome

*Tuberculosis* is discussed in another section but is worthy of brief comment because of the fact that it may be readily confused with regional enteritis The commonest site of intestinal tuberculosis is the lower ileum and cecum The most common form is that of an infiltrating process with superficial ulceration of the ileum In the cecum progressive granulomatous change may occur with marked thickening of the wall and the formation of a tumorlike mass, which may resemble carcinoma The symptoms are those of irritation of the lower small bowel with diarrhea periumbilical or right lower quadrant cramplike pain and the finding of occult blood in the stools Associated with these symptoms there may be loss of appetite and weight with an accompanying anemia Physical examination may reveal a local tender mass in the vicinity of the cecum with evidence of peritoneal irritation as shown by muscle spasm A much less common form of tubercular involvement is *that of local hypertrophic change* with stenosis and gradual obstruction of the terminal ileum In many instances of tubercular enteritis evidences of present or past pul

monary tuberculosis will be found Occasionally it will be impossible to demonstrate the existence of tuberculosis in any other part of the body Rarely the appendix may be involved in the tuberculous process and the presenting symptom may be that of appendiceal pain In the ulcerative form perforation and fistula formation constitute a moderately frequent complication Diagnosis must be based on an adequate history objective physical findings and a careful x ray examination first by barium enema and subsequently by small bowel studies Tubercle bacilli may be found in the stools but this represents an inconstant finding Evidences of tuberculosis elsewhere in the body may provide confirmatory evidence of the disease Because of the location of the lesions the first consideration in differential diagnosis is that of regional enteritis which will be discussed below In the absence of symptoms of obstruction or of fistula formation conservative medical measures with adequate rest a nonirritating diet of low roughage content and antispasmodics should be employed At times tincture of opium and bismuth preparations may be helpful in reducing the number of bowel movements Where the diagnosis is proved streptomycin therapy may be very effective It probably should not be combined with para amino salicylic acid if diarrhea is a marked feature Where obstruction and fistula formation are present surgical resection may be indicated

REGIONAL ENTERITIS —Regional enteritis may be classified as a nonspecific granulomatous disease of the small bowel usually involving one or more segments of the terminal ileum The disease is chronic with remissions and exacerbations and may be entirely asymptomatic the diagnosis being made by accident at the time of abdominal exploration for other disease Pathologically the lesions are those of proliferating granulomata involving primarily the mesenteric border of the small bowel in a single segment or in multiple areas Skip areas are common and in severe cases not only may the jejunum and ileum be involved but occasionally the duodenum as well In a small percentage of cases the disease involves the cecum and the colon in which event the term ileocolitis is usually employed The *etiology* of the disease is not known It bears a close clinical relationship to tuberculosis but it is quite certain that it is not due to this specific infectious agent

The *symptoms* of the disease vary It may be ushered in by an acute febrile attack with the sudden onset of right lower quadrant cramplike pain an elevated temperature and leukocytosis Such an episode is usually mistaken for an acute attack of appendicitis but at operation the characteristic pathological findings of enteritis may be found, in this instance usually well localized to the terminal ileum In other cases the history is that of recurrent episodes of periumbilical or right lower-quadrant cramps with diarrhea slight elevation of temperature and occasionally nausea and vomiting Moderate leukocytosis may be present and the stools may show occult blood *Physical examination* may be entirely negative but almost always reveals right lower-quadrant tenderness some muscle rigidity occasionally rebound tenderness and a palpable mass in the region of the cecum The mass may be easily defined and may be as large as 6 to 7 cm in diameter or it may be distinguished merely as an indeterminate mass characteristic of an inflammatory process Occasionally it is in the low midline rather than in the right lower quadrant In the chronic cases fistula formation may be evident either because of the appearance of the fistula in the abdominal wall or because of the finding of fistulous tracts on subsequent roentgenological examination In the chronic form of the disease appetite may be diminished and the intake of food definitely reduced because of the fear of producing increased diarrhea and abdominal pain Serious loss of weight and severe nutritional disturbances may be encountered The stools are characteristically semi solid rather than liquid containing excessive mucus and on microscopic examination show pus and red cells gross blood may occasionally be present *Differential diagnosis* must include the possibility of ulcerative colitis tuberculous enteritis new growth or in the acute cases acute appendicitis Sigmoidoscopic examination will be essentially negative except for signs of irritation of the rectum and recto

sigmoid, without any evidence of ulcerating lesions Mucopurulent or bloody discharges may be noted coming down from above during sigmoidoscopy A barium enema will frequently show a characteristic and persistent narrowing of the terminal ileum as barium refluxes through the ileocecal valve and produces the so-called "string sign" In most instances the cecum will be normal, but in some cases, cecal involvement may be present, and, as already indicated, there may occasionally be involvement of the remainder of the colon A small-bowel study by *x* ray will demonstrate a permanent deformity or narrowing with irregularity of the normal pattern in the terminal ileum and where the disease is widespread it will usually indicate skip-areas" at higher levels with or without evidences of obstruction If obstruction is present dilated loops of small bowel are always found above the obstructing area Fistulæ may be demonstrable either by barium enema or by small bowel series In the absence of other evidences of tuberculosis, the diagnosis of regional enteritis may be made with reasonable certainty particularly if numerous areas of the ileum are involved

*Treatment* —The treatment of this disease is far from satisfactory It has been reviewed particularly by Crohn and Garlock whose experience with the condition has been extensive Inasmuch as there is no known specific etiological factor medical therapy cannot be said to be in any way definitive The results of surgery are still somewhat controversial In the opinion of the author, conservative measures would seem to be indicated in the absence of proved obstruction or fistula formation and in cases in which symptoms are recent and involvement is limited to a small segment of the ileum Such a conservative attitude may be justified by the fact that, occasionally, completely asymptomatic and apparently healed lesions are found in the course of abdominal exploration for other disease and also by the fact that certain cases seem to have responded well to such conservative measures over a period of many years If medical treatment is to be carried out then the principles of long-continued rest and the administration of a low roughage highly nutritious diet are fundamental considerations Chemotherapy and the use of antibiotics has not been universally successful In some instances a course of sulfadiazine followed by the use of sulfathalidine over a period of weeks or months appears to have been of real benefit Penicillin is of no value Streptomycin may be of help during acute manifestations of the disease and on occasion the use of chloromycetin seems to have

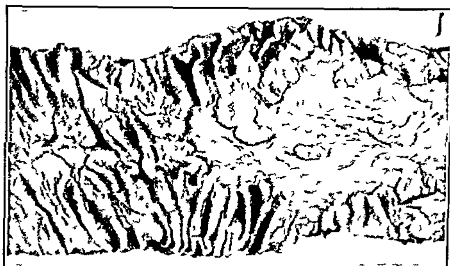


FIG 204 —Regional enteritis illustrating a sharp demarcation between healthy and diseased bowel irregular ulcers and prominent residual islands of mucosa (Herbut s Surgical Pathology )

been followed by beneficial results particularly in the cases with elevated temperature and toxic manifestations. Aureomycin and terramycin are probably contraindicated because of their tendency to cause diarrhea. Mild sedation with the barbiturates and at times the use of atropine or its derivatives are helpful.

Failure to respond to consistent carefully carried-out medical measures undoubtedly should lead to a decision in favor of surgical intervention. The only contraindication to operative interference is the presence of diffuse involvement of the jejunum and ileum which precludes any successful surgical maneuver. In the event that surgical intervention is considered indicated a short-circuiting operation with the performance of an ileotransverse colostomy is the procedure of choice. Combined with this maneuver a resection of the diseased ileum together with the ascending colon may be indicated either because of fistula formation with resulting abscess or because of continuing evidence of disease in that portion of the bowel which was supposed to be put at rest by the short circuit. One of the very real difficulties attending surgery for regional enteritis is the fact that skip areas may evade detection at the time of operation with the result that the disease reappears in active form above the anastomosis. Attempts at radical resection of numerous areas of disease is usually attended by unsatisfactory results. Occasionally local areas of obstruction may require enteroanastomosis for symptomatic relief.

Recurrences may occur either under medical management or after what seems to be properly indicated surgery. Because of the nutritional disturbances that frequently accompany this condition dietary supplements in the form of vitamins and possibly liver extract may be of some benefit. The ultimate prognosis in regional enteritis is never clear in individual cases. In instances in which favorable results are obtained during initial therapy it is of the utmost importance to train the patient in future proper dietary habits as well as in the proper regulation of his life in order to resist the effects of emotional stress and strain, excessive fatigue and intercurrent infection.

## THE SPRUE SYNDROME

Sprue or psilosis is a chronic disturbance of the small bowel characterized by faulty absorption of lipoids and other nutrient elements. The exact etiology of the condition is not known but the response to specific factors such as liver extract, vitamin $B_{12}$ and folic acid, has properly led to the assumption that it is primarily a deficiency disease. The brilliant therapeutic results obtained by Castle and Rhoads following the administration of liver extract and the subsequent demonstration by these authors, Spies and Suarez of the efficacy of vitamin $B_{12}$ and folic acid would certainly point towards such a conclusion. However the fundamental physiologic disturbance exhibited by patients with the sprue syndrome is that of impaired intestinal absorption and it is quite possible that the deficiencies exhibited may be the result rather than the cause of the manifestations of this interesting condition. As partial support for the idea that the syndrome is primarily due to an inherently impaired absorptive function one may cite the fact that it is not at all infrequent to obtain a history from adult patients of earlier nutritional difficulties that have been diagnosed in childhood as celiac disease. For years an attempt has been made to differentiate between cases of so-called tropical sprue occurring in tropical and subtropical areas and cases of sprue encountered in temperate zones which have been classified as nontropical sprue. Such a differentiation is probably an arbitrary one although there is little doubt that the condition is encountered with much greater frequency in the warmer latitudes. Reports by Thayson, Snell, Hanes, Suarez and others would seem to indicate that the syndrome is fundamentally the same wherever encountered although the clinical manifestations may be subject to modification depending upon climate and upon economic and environmental conditions. The identity of tropical sprue, nontropical sprue and celiac disease has been stressed by Hanes and others. The clinical manifestations of this condition and its treatment have been described in Chapter 11. Because the sprue syndrome is fundamentally associated with

impairment of small intestinal absorptive function, it is pertinent to comment briefly on recent therapeutic developments. In cases that have been extremely intractable to the prolonged use of liver extract, vitamin $B_{12}$, and folic acid, dramatic improvement in *intestinal absorption with* subsequent amelioration of all the symptoms of the disease has been achieved by the use of the corticosteroids. Balance studies carried out by this writer and his group, by Wollaeger and by Almy indicate clearly that the use of ACTH or cortisone has been associated with *a striking reduction in the fat content of the* stools, together with disappearance of diarrhea and distention and accompanying evidence of improved general intestinal absorption. It may well be that the use of corticosteroids will provide a valuable addition to our means of controlling this disease in its later stages and, incidentally, serve to increase our understanding of the underlying physiological disturbance.

## APPENDICITIS

Appendicitis is essentially a surgical condition and is the result of an acute inflammatory involvement of the vermiform appendix. It may occur as a single acute attack or may recur at intervals as mild attacks without definite recognition. The *etiology* of the condition would seem to be associated with two factors: fecal stasis with more or less obstruction to the lumen of the tubular *structure,* and infection behind the obstructed area. Infection may be caused by the multiplications of organisms normally contained in the intestinal flora or may be associated with a streptococcal *infection incident* to acute respiratory disease.

*Symptoms.*—The symptoms of appendicitis are classically those of pain, tenderness and spasm in the right lower quadrant. The localization of symptoms may vary, however, with the exact location of the appendix so that both pain and tenderness may be noted in the right flank, in the event that the appendix is retrocecal, or symptoms and signs may be localized in the low mid hypogastrium or in *the pelvis.* At the onset of an attack, the initial symptom is usually that of epigastric pain, with nausea and, possibly, vomiting. As the attack progresses the pain characteristically descends to the right lower quadrant, *and tenderness to palpation* appears at or near a point midway between the iliac crest and the umbilicus (McBurney's point). In an acute attack suggesting the possibility of appendicitis, it is important to remember that tenderness to palpation may be found only by rectal or vaginal examination. In older patients pain may be entirely absent and the condition may be suspected only because of an acute upset with nausea and vomiting and with a subsequent *rise in temperature and local ab*dominal tenderness. The sudden disappearance of pain always suggests perforation of the appendix with a local peritonitis.

*Diagnosis.*—Physical examination, in addition to demonstrating local tenderness, may exhibit rebound tenderness and usually shows muscle rigidity, which is evidence of peritoneal involvement. This is one of the most valuable signs of the condition. Fever is nearly always present; it may be only *moderately elevated or may be between 103* and 104 degrees Fahrenheit. Chills occur infrequently. Leukocytosis is nearly always present with an increase in the polymorphonuclear leukocytes. Except in children where higher counts are to be expected, a white count of over 20,000 cells per cubic millimeter should suggest the possibility of perforation. Differential diagnosis should include consideration of acute cholecystitis, right renal calculus, acute salpingitis, ectopic pregnancy, torsion of an ovarian cyst, ruptured graffian follicle, right lower lobe pneumonia, and acute attacks of gastroenteritis. In older individuals rupture of an *infected diverticulum of the sigmoid,* although usually left sided, may closely resemble an attack of acute appendicitis. In pneumonia of the right lower lobe with pain referred from the diaphragm, the picture may be confusing particularly in children, but, as a rule, one can easily demonstrate that pain is dependent upon respiration and ceases or is almost entirely absent when the patient holds his breath. Furthermore the lack of rebound tenderness or tenderness on rectal examination provides additional information. In the event that perforation of the appendix has occurred, one additional

symptom may be the development of diarrhea which may be the presenting symptom when the patient is seen In this event diagnosis can be made primarily on physical signs alone

*Treatment* —Diagnosis should be made as quickly as possible and should be followed by surgical removal of the appendix Conservative measures and medical treatment rarely are justified It is of extreme importance to avoid the use of laxatives if the diagnosis of appendicitis is *considered possible* and nothing should be given by mouth until the diagnosis is certain In older people or in young children replacement of fluid and electrolytes may be of importance as part of preoperative preparation Where perforation *is suspected with resulting peritonitis* the use of antibiotics particularly penicillin and streptomycin is indicated With prompt diagnosis and treatment the prognosis is good Where the diagnosis has been delayed or where perforation has occurred the outlook depends upon the degree of peritoneal involvement and the measures instituted for its control

*Chronic appendicitis* is a diagnosis that should be avoided since it probably does not exist in any true sense There is little doubt that recurrent attacks of mild appendicitis occur and may eventually be recognized as such But that a truly chronic inflammatory process which is the cause of lower abdominal symptoms occurs is very much to be doubted

## DISEASES OF THE COLON

Disturbances of the colon may be due primarily to abnormalities of motor and secretory function or as in other portions of the digestive tract may be associated with *congenital malformation tumors or inflammatory* disease

### MOTOR AND SECRETORY DISTURBANCES

MUCOUS COLITIS —Excessive *motor and* secretory activity of the large bowel may be appropriately considered under the term mucous colitis or irritable colon The syndrome of mucous colitis consists essentially of gastrointestinal symptoms predominantly referable to the colon It was originally described in a classical article by Da Costa and has subsequently been studied in careful detail by Bockus Friedenwald, White, Jordan and many others

The *symptoms* of this condition are primarily referable to the colon and at one time or another include episodes of constipation or diarrhea accompanied by ab*dominal pain and the passage of stools of* small caliber In the majority of instances the first symptom is that of constipation which typically appears in the second or the third decade Diarrhea is a somewhat later development and may alternate with periods of constipation Characteristically there is a history of the passage of long strings of mucus or of mucous casts of bowel with extreme hypogastric pain In periods of constipation the movements may be hard or soft If hard scybalous masses are passed rectal and anal discomfort may be extreme At times ribbon or pencil like stools are noted indicating increased muscular spasms of the rectal segment and of the anal musculature Pain in most instances is hypogastric and most frequently over the location of the lower descending colon and sigmoid Associated symptoms may include upper abdominal complaints such as heartburn belching epigastric fullness *etc* , and in addition it is common to obtain evidences of autonomic instability such as tachycardia excessive sweating easy fatigability and the like *Lower abdominal pain is* nearly always associated with bowel movements The taking of cathartics almost invariably increases the intensity of the pain as does the ingestion of coarse foods with a high cellulose content A careful history will usually elicit the fact that increased nervous or emotional tension also aggravates symptoms with production of constipation or diarrhea and abdominal discomfort Passage of blood may occur even in the absence of anal fissure or hemorrhoids It is usually noted as streaks of blood on the outside of the stool but may be associated with the passage of larger amounts of red blood although this is a rare occurrence

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as agar or Irish moss may be of extreme help. These preparations should not be used unless at the same time great stress is laid upon the attempt to establish proper bowel habits. When very striking irritation of the bowel is evident on the basis of symptoms or sigmoidoscopic examination preparations of vegetable mucins act as a demulcent and may be employed effectively. For the cramplike pains that at times are extremely severe the use of antispasmodics and of sedatives may be extremely effective. Atropine belladonna or banthine in *tolerance* doses may be employed over variable periods of time and the additional use of the barbiturates in small repeated doses may relieve not only the underlying nervous tension but also the bowel spasm which is a reflection of this tension. Among other important therapeutic details it is of extreme value to plan a program of activity and periodic relaxation that makes it possible to avoid both physical and nervous fatigue. The care of patients with mucous colitis requires endless patience and time but persistent treatment frequently results in alleviation of symptoms and a well-controlled patient.

Atony of the Bowel.—Atony of the bowel may result from various causes. It may be the direct result of an associated peritonitis in which event abdominal distention and the absence of peristaltic sounds and any peristaltic activity will reveal a total lack of intestinal motor function. It is an ominous sign of serious abdominal disease and usually involves both the small and the large bowel. Although the treatment must be primarily directed toward care of the fundamental disorder the distention encountered in the presence of peritoneal irritation may be dramatically reduced by the inhalation of high concentrations of oxygen. Morphine sulphate may also give relief by increasing the tonicity of the gut. Such an atonic distended bowel has no real propulsive activity and in addition serves as a reservoir for important quantities of unabsorbed fluid electrolytes and nutrient material which may further hazard the prognosis of the patient. Therapy must therefore include proper replacement of fluid and electrolytes. Similar atony of the bowel may occur as a result of injury to the spinal cord from trauma or tumor and may also be an accompaniment of syphilitic involvement of the cord. Under such circumstances complete motor activity may not be abolished but normal propulsive movements do not occur and spontaneous evacuation of the bowels becomes extremely difficult. The use of carefully administered saline or oil enemas or of skilfully performed colonic irrigations may be of real assistance in solving the problem until normal bowel activity is at least partially restored. In debilitated individuals particularly those suffering from episodes of severe systemic infections the muscular tone of the bowel frequently becomes diminished. Proper evacuation is retarded both from this cause and as a result of loss of strength in the abdominal musculature which normally provides additional intra abdominal pressure aiding bowel emptying. Such an occurrence is not infrequently seen in instances of poliomyelitis with paralysis of the muscles of the trunk and abdomen. In older individuals who have long suffered from faulty bowel habits and accompanying constipation there may be a gradual loss of colonic tone with slowly progressing distention of the bowel from retained fecal material. Bowel evacuation becomes increasingly difficult and must be aided by the careful use of enemas or of mild cathartics such as cascara or senna or the saline purgatives. Where distention is extreme the use of physostigmine or prostigmine may be temporarily effective. It should be remembered that in this group of older persons fecal impaction of major degree may occur with resulting overdistention of the bowel and the passage of loose watery movements which represent small bowel contents that have slipped past the masses of retained feces. In such instances diarrhea may be the presenting symptom but the cause is properly described as obstipation. Abdominal distention due to dilatation of the large bowel should never be considered as evidence of primary atony of the bowel musculature until a thorough search has been made for a possible cause of colonic obstruction such as an annular carcinoma or diverticulitis.

Almost invariably, certain specific personality characteristics are apparent in patients suffering from this clinical syndrome They are definitely overreactive individuals frequently overconscientious, and highly dependent upon the opinions of others Emotional tension is nearly always an obvious fact and frequently dominates the picture Anxiety guilt, and resentment are the most common emotional states associated with the nervous tension apparent in all these individuals

*Physical examination* usually reveals general nervous excitability with hyperreflexia Not infrequently there are well marked flushing of the skin cold moist extremities and an exaggerated wheal response Almost invariably, the descending colon and upper sigmoid can readily be felt as a firm tubular structure, which is tender to deep palpation Rectal examination may reveal a tight anal sphincter, and hemorrhoids or fissures are not uncommon because of the persistence of constipation or diarrhea Other physical findings of importance are lability of pulse rate and irregular sighing respiration

*Diagnosis* —In addition to a careful history and the demonstration of autonomic-nervous system instability by careful physical examination the most important diagnostic procedure is that of sigmoidoscopy The sigmoidoscopic findings have been most carefully described by Friedenwald and his associates In the early stages of the condition or in the milder cases sigmoidoscopic examination reveals generalized hyperemia and injection of the rectal and rectosigmoidal mucosa with excessive secretion of fresh mucus and extreme irritability to touch Transient spasm may make sigmoidoscopy difficult, but avoidance of a hurried examination will permit the passage of the instrument to its full length In the most severe cases, all these signs are strikingly increased with the excessive production of mucus which is frequently thick and tenacious and is detached from the mucosal surface only with difficulty Careful wiping of the mucosa may reveal very fine granularity but ulceration is not seen Radiological studies are of importance only to exclude other conditions A barium enema may show transient areas of spasm but its chief importance is to demonstrate the absence of signs of ulceration, new growth or diverticulitis The appearance of gross blood in the stools has already been noted Such a finding may occur, but extreme care should be taken to exclude all other possible sources of bleeding before accepting the fact that rectal bleeding may result solely from the hyperemia and increased vascularity typical of this condition

At times the clinical picture of mucous colitis may be closely simulated by true gastrointestinal allergy Although this is a relatively infrequent occurrence a careful allergic history is always indicated

*Treatment* —The condition known as "mucous colitis" or "irritable colon" is extremely common, and because of the severity of the symptoms warrants careful consideration and a carefully planned therapeutic program based on the understanding that all the symptoms are fundamentally associated with an exaggeration of the normal physiological activity of the bowel Once adequate assurance has been obtained that no serious organic disease is present treatment should be directed toward reassurance and the management of the patient as a disturbed, harrassed individual Psychotherapy may at times be of extreme importance, but in many instances, an understanding physician can adequately handle the situation with patience kindness and attention to minor details Sources of anxiety and tension should be searched for fully discussed and, if possible removed or avoided Dietary measures are of importance inasmuch as coarse irritating foods very definitely aggravate symptoms The diet should be chosen with this point in view At times high roughage foods should be entirely avoided or if used should be strained Attention to the regulation of bowel habits is of extreme importance inasmuch as many of these patients are convinced that cathartics are indicated Careful reconstruction of bowel habits is absolutely essential Cathartics should be avoided as well as the use of enemas except in rare instances where the periodic use of an oil retention enema may result in the easier evacuation of hard bowel contents At times the use of mineral oil or of oily combinations with such substances

Physical examination reveals abdominal distention and very often huge fecal masses can be palpated through the abdominal wall. Unless aided by the use of enemas or laxatives bowel movements may occur only at prolonged intervals of many days or weeks. In young children the condition may lead to poor physical development and inadequate nutrition. Abdominal cramps may be present and sometimes though not often nausea and vomiting which are essentially on an obstructive basis. In the milder forms of this disorder fairly adequate bowel activity may be obtained by the use of laxatives or numerous enemas; occasionally physostigmine or prostigmine may be helpful. As the condition develops however surgical intervention may be necessary. Various surgical procedures have been employed including extirpation of the colon and section of the lumbar sympathetic nerves. The recent work of Swenson provides the most hopeful approach to this difficult problem. In a series of patients with congenital megacolon he has found that resection of the lower colonic segment which is poorly supplied with intrinsic nerve fibers and an anastomosis of the distal end of the transected colon to the terminal rectal segment may provide a very satisfactory therapeutic result.

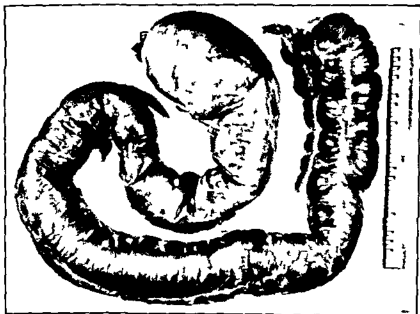


Fig. 205.—Congenital megacolon removed from a boy three years old. (Herbut's Surgical Pathology.)

Diverticulosis.—Diverticulosis of the colon is a very common finding. It probably represents a developmental defect in focal areas particularly in the sigmoid and descending colon with a gradual pouching out of the weakened abdominal musculature until demonstrable diverticula are formed. It is estimated that demonstrable diverticulosis of the colon may be present in 5 per cent of otherwise normal adults. In most instances the condition causes no symptoms, and the diagnosis is made by accident during the course of routine x-ray examination of the gastrointestinal tract. In a moderate number of individuals usually in the middle or later decades of life inflammation of the diverticula may occur and the term *diverticulitis* may appropriately be employed. Such an inflammatory process may occur as a single episode or may be present as a chronic inflammatory process with recurrent symptoms. In an acute episode a definite change in bowel habits occurs which may be marked either by constipation or by diarrhea. It is associated with lower left-quadrant pain and tenderness inasmuch as diverticula located in the sigmoid are most commonly

CONSTIPATION AND DIARRHEA.—Both constipation and diarrhea may occur as symptoms of disturbed motor function that is *entirely independent of structural or organic disease of the bowel.* The term *constipation* should be used to describe a *condition in which bowel activity is retarded* and is accompanied by the passage of hard firmly packed fecal masses. The term *diarrhea should be used to describe a condition in* which there is the passage of frequent, liquid movements. Either condition may be *associated with organic disease or with a* clinical syndrome, such as mucous colitis. However, either condition may be the result *merely of faulty bowel habits, nervous tension,* or endocrine disorders such as hyper- or hypothyroidism, diabetes, pituitary *dysfunction and the like.* Thus hyperthyroidism is commonly associated with increased bowel activity and frequent movements. The movements may be liquid in character or may consist merely in the frequent passage of fairly well formed stools. Myxedema is typically accompanied by sluggish bowel activity with at times rather obstinate constipation. Diabetes, for reasons not fully understood, may be accompanied by the passage of frequent, loose stools. In pernicious anemia and in gastric achlorhydria diarrhea is occasionally an important symptom.

By far the most common cause of constipation is a failure to establish and maintain regular bowel habits. This is a most important point to be emphasized inasmuch as the use of cathartics in such instances is usually not indicated and the condition can be corrected by persistent attempts to regulate the hours of eating, the taking of an adequate amount of fluid, and the establishment of an invariable and regular time for going to the toilet. Where constipation is of long standing the use of oily *preparations or of* mild cathartics may help to initiate bowel movements at a given time of day, but the continued use of these *preparations* is to be discouraged.

Diarrhea may occur merely as the reflection of a good deal of nervous and emotional tension. The characteristic of this type of diarrhea is that almost invariably the bowel movements occur only in the waking hours. As a rule the movements come in the morning before and after breakfast and again after the intake of food at other times during the day. Loss of weight and malnutrition are rarely present even *though bowel movements may* occur as many as eight to ten times during the day. The condition is aggravated by excitement, emotional tension, and frequently by the use of iced drinks, excessive amounts of alcohol and coarse foods. In addition to attempts to modify the emotional tension *that is* present, therapeutic measures may properly include the use of small repeated doses of tincture of opium with or without *tolerance doses of belladonna* in order temporarily to slow down bowel activity and diminish bowel irritability. Where nervous *diarrhea is of long standing these drugs may* properly be employed over a period of many weeks in order to break into what is essentially a *vicious cycle.*

## CONGENITAL ABNORMALITIES

Congenital abnormalities of the colon present two widely divergent conditions: megacolon and diverticulosis.

MEGACOLON (HIRSHSPRUNG'S DISEASE).—This condition is usually found in children and presents a remarkable and extreme dilatation of the large bowel. The dilatation may extend to the internal sphincter of the anus but more commonly ends at a slightly higher level. The mechanism underlying this condition is not completely clear, but recent investigations by Swenson indicate that in a large proportion of cases there is a distinct abnormality of the intrinsic innervation of the bowel wall just proximal to a *terminal segment which is quite normal.* This abnormality consists in the absence of Auerbach's plexus in the rectosigmoid. As a *result of this faulty innervation of the lower colon, propulsive movements are* ineffective or absent, with resulting failure to move material from the upper levels of the bowel downward through the distal segment into the anal canal. As a result the child or young adult provides a history of steadily increasing difficulty in bowel evacuation with increasing abdominal distention due to the dilatation of the entire colon

but when it is encountered it may be profuse and sufficient in degree to produce serious blood loss. A definitive diagnosis must depend upon careful radiological studies by barium enema. In most instances no difficulty is encountered in establishing the presence of diverticula and the existence of associated spasm when an inflammatory process is present. Occasionally the deformity and the narrowing of the sigmoid colon cannot be distinguished from an infiltrating malignant lesion.

*Treatment* in the milder cases consists in the use of proper dietary measures, antispasmodics and morphine for the control of pain and soothing retention enemas. In relatively acute cases the diet must consist entirely of foods with small residue. Atropine or its derivatives in therapeutic doses may be of additional help in relaxing a certain amount of spasm and in relieving cramplike pains. Where pain is severe morphine is indicated. Chemotherapeutic agents are probably of little help unless there is evidence of a peritonitis associated with perforation. In an acute or subacute attack the use of small hot (115–120 degrees Fahrenheit) oil retention enemas may provide striking symptomatic relief. Cathartics and laxatives are contraindicated. In the very acute attack that suggests perforation with peritoneal involvement surgical intervention is necessary. Where obstructive symptoms are marked and of long duration or attacks occur with increasing frequency, resection of the involved area of the bowel must be carried out. Furthermore if it is suspected that the lesion may be malignant, a similar procedure is mandatory. In patients with recurrent mild symptoms adequate control may be obtained by low roughage diets, the use of small frequent doses of mineral oil and at times the use of antispasmodic drugs.

## TUMORS

About a third of all the tumors occurring in the gastrointestinal tract are to be found in the colon. Somewhat more than half of these represent benign conditions but malignant tumors of the large bowel are among the most frequent tumors in the body.

Benign Tumors.—The most common benign tumors of the large bowel are adenomata and lipomata. Adenomata may occur as single tumors in any part of the large intestine. They may be multiple occasionally; they are present as a diffuse generalized polyposis of the entire colon. The adenomas appear as polypoid masses which are pedunculated or sessile. The pedunculated tumors may have a rather long vascular stalk and when located in the region of the sigmoid may produce symptoms of obstruction. Adenomata may occur in the earlier decades of life or may be acquired in the later decades of life, possibly secondary to chronic inflammatory disease. All adenomatous polyps are potentially malignant. Where there is generalized polyposis of the entire bowel there is frequently a familial incidence of the condition. When such a case is encountered it is advisable to examine the siblings of the patient and possibly other members of the family inasmuch as the condition is always associated with carcinomatous degeneration. Lipomata as well as the less common fibromata, myelomata and hemangiomata may also appear as polypoid masses, either sessile or pedunculated.

*Symptoms.*—The symptoms caused by any of these benign tumors are due to bleeding or to interference with normal bowel activity as a result of partial obstruction or intussusception. Hemorrhage from benign tumors of the bowel is common and may occur without any other symptom. Recurrent attacks of lower abdominal cramping pain with diarrhea or constipation are frequent and evidences of bleeding nearly always accompany such disturbances. Progressive anemia may be present and where malignant degeneration has occurred loss of weight and strength are accompanying features.

*Diagnosis.*—The diagnosis of benign tumors is based on the history of bleeding, on episodes of lower abdominal pain and on adequate sigmoidoscopic and radiological studies. If anemia is practically the only presenting sign and occult blood in the stools has been demonstrated sigmoidoscopy and examination of the colon by barium enema are essential measures. Very fre-

involved in an inflammatory process Physical examination—or rectal examination if a lower segment is affected—will reveal a tender mass in the left lower quadrant over the course of the sigmoid In milder cases, the symptoms may be less striking and may be initiated by gross indiscretions in diet by lack of regulation of bowel habits, by extreme fatigue or nervous tension with resulting changes in bowel activity or by intercurrent infection In any event the pain or discomfort is characteristically located over the course of the involved bowel and *physical signs* are as described above When spasm of the sigmoid is extreme because of the local inflammatory process which may include tremendous thickening and edema of the bowel wall, the symptoms and signs may be those of large bowel obstruction Fever and leukocytosis may be present In very acute attacks, perforation of a diverticulum with the formation of a pelvic abscess, may occur Such attacks at times simulate acute appendicitis, although in most instances the pain and tenderness is on the left Fistula formation may develop between the sigmoid and the urinary bladder In milder cases bladder symptoms are not infrequent, and, at times, the patient complains primarily of bladder irritability and frequency of micturition



FIG 206 —Diverticula of the colon demonstrated by a barium enema Note the bud like projections as indicated by the arrows (Holmes and Robbins Roentgen Interpretation )

In most instances the *diagnosis* can be made by careful history and physical examination but in every instance the physician must rule out the possibility of carcinoma The coexistence of carcinoma of the sigmoid and diverticulitis is not rare It is probable however that chronic diverticulitis *per se* does not lead to the development of malignant degeneration Bleeding rarely occurs

fluid material frequently mixed with blood There may be an alternation of diarrhea and constipation Profound anemia is a characteristic finding in tumors of the right side of the colon, probably due to the fact that diagnosis is more frequently deferred because of the absence of obstructive symptoms In the descending colon the rectosigmoid and the rectum obstructive symptoms are common and consist in increasing difficulty in evacuation of the bowels lower left abdominal cramping pains distention and the passage of fresh blood and mucus in the stools Loss of appetite is frequent and nausea and vomiting are common accompaniments of left sided cancer

Physical examination usually reveals evidence of anemia and loss of weight Abdominal distention is not uncommon and, in a large percentage of cases a palpable tumor mass may be felt either by abdominal palpation or by digital examination of the rectum Too great emphasis cannot be placed on the fact that the vast majority of rectal cancers can be felt with the examining finger There is no reasonable excuse for failing to make a careful digital examination on any patient complaining of the passage of fresh blood in the stools

*Diagnosis* of malignant disease of the colon is usually easy If rectal examination does not readily disclose a tumor sigmoidoscopy should be performed before radiological studies are made By means of sigmoidoscopy, a tumor may be demonstrable within the range of the instrument but beyond the reach of the examining finger If no tumor is seen it may nevertheless be possible to observe bloody material coming down to the mouth of the scope which indicates an ulcerating lesion at a higher level If digital and sigmoidoscopic examinations are negative then a barium enema should be given for a study of the higher levels of the large bowel In most instances little difficulty will be encountered in localizing the deforming lesion Occasionally in the presence of partial obstruction radiological study may



Fig 208 —Cancer of sigmoid Note irregular area of stenosis with shelf like appearance above and below narrowed portion of bowel

quently single sessile or pedunculated polyps may be seen just at the upper limit of sigmoidoscopic examination. They may be beyond the reach of the instrument, however, and are then to be searched for by means of a barium enema. Occasionally, they can be demonstrated only by so called double-contrast enemas.

*Treatment.*—Treatment of benign tumors of the colon is surgical. Although there is no exact knowledge of the percentage of malignant degeneration of benign polyps, the only reasonable course is to insist upon removal whenever polyps or other benign tumors are demonstrated, either by local fulgeration through a sigmoidoscope when the tumors are limited to the rectum or by actual excision or resection of the affected bowel area, when the tumors are found at higher levels. At the present time total colectomy would seem to be the only reasonable procedure in the treatment of generalized polyposis.

MALIGNANT TUMORS.—With few exceptions malignant tumors of the colon are carcinomatous. Infrequently, colonic malignancy may be on the basis of sarcomatous infiltration, usually classified as lymphosarcomatous. More than half of all carcinomata of the large bowel are to be found in the rectum and rectosigmoid. Carcinomatous tumors may be present as large, ulcerating cauliflowerlike masses, or may be annular in type, with partial or almost complete obstruction of the lumen of the bowel. A third type, colloid carcinoma, is characterized by a large tumor mass with abnormal production of mucinous material. The colloid form of carcinoma is most frequently found in the region of the cecum or the right colon. The scirrhous type of carcinoma occurs most commonly in the rectum and rectosigmoid.



FIG. 207.—Cancer of cecum. Note irregular moth eaten appearance of involved area.

*Symptoms.*—There is a striking difference between the symptoms of malignancy in the right half of the colon and that encountered in the left portion of the bowel. Obstructive symptoms are usually lacking in cecal or right-colonic malignancy. Diarrhea is common, with the passage of large amounts of

be fatal in a few weeks without the convincing demonstration of any pathogenic organism. Persistent ulcerative colitis may be associated with chronic amebic dysentery but may persist after all evidences of amebic infestation have disappeared with successful antiamebic therapy. A point worthy of note is that the vast majority of individuals suffering from idiopathic ulcerative colitis are essentially overreactive, immature, highly dependent and insecure. Indeed at times the psychological aspects of the condition may be dominant and cumulative emotional disturbances may appear to have precipitated the condition. Until definitive proof is obtained of a single specific etiological factor, it is wise to consider nonspecific ulcerative colitis as a condition which is the result of varying types of insult to the bowel occurring in individuals who are peculiarly unstable from the psychological point of view.

In typical cases the pathological process involves first the rectum and rectosigmoid and subsequently, the remainder of the colon up to the ileocecal valve. In a small percentage of cases the disease may be characterized by a regional distribution of the lesions in either the ascending or the transverse colon, but in such instances there is no assurance that the disease will not progress downward toward the rectum. Involvement of the terminal ileum does occur but in relatively few cases. A point of confusion is due to the fact that some cases of regional enteritis involve not only the terminal ileum but also the colon and run a course almost identical to that of typical ulcerative colitis. The initial lesions of the disease are usually readily seen on sigmoidoscopic examination and are characterized by the presence of minute superficial bleeding points throughout the mucosal surface with hyperemia, swelling and great friability. In this stage of the disease the diagnosis may frequently be missed if the mucosal surface is not carefully wiped during sigmoidoscopy, inasmuch as it is common to find a layer of shiny mucus overlying the entire area and giving it the appearance of an almost normal rectal or rectosigmoidal surface. Invariably gentle wiping with a sponge will reveal the lesions described above and a finely granular irregular surface. At this stage the lumen of the rectum or rectosigmoid may be of normal size but it is always extremely irritable and exhibits spasmodic contraction to contact. Occasionally, the process is limited for years to the rectum alone or to the rectum and lowest segment of the rectosigmoid but it must be remembered that the situation may change abruptly from one of apparently superficial localized disease to a diffuse fulminating process involving the entire colon. As the disease progresses, sigmoidoscopic examination reveals narrowing of the lumen of the bowel with marked edema and stiffness. Granularity becomes coarser and superficial ulcers ranging from 0.5 to 2.0—3.0 mm. in diameter may be seen. Serpiginous ulcers are sometimes encountered and when noted, should raise the question of tuberculous involvement. In the late stages of the disease involvement of the entire colon occurs with eventual ulcerative denudation of the mucosa and fibrous thickening from scar tissue. At this point x-ray examination of the bowel reveals so-called pseudopolyps which in most instances are composed of small areas of fibrous tissue or remnants of mucosa. Eventually the entire bowel becomes a thickened fibrous tube of small caliber. In the very acute stages of the disease tremendous thickening of the bowel wall may occur, equivalent to a phlegmonous cellulitis.

Perforation of ulcers fortunately is not common, but it may occur at any time in the very active stages of the disease leading to local abscess formation, peritonitis or fistulous tracts communicating with the abdominal wall, the small bowel or the vagina. Other immediate complications of the disease are the development of anal fissures, hemorrhoids, perianal abscesses, periurethral abscesses and osteomyelitis of the sacrum or coccyx.

Other more distant complications of the disease are the development of various deficiencies, joint manifestations, the appearance of cutaneous lesions, clubbing of the fingers and hepatic changes. Evidences of deficiency disease range from the typical manifestations of the various avitaminoses to profound dehydration, electrolyte im-

reveal only a narrow area beyond which barium does not pass. This in itself gives sufficient evidence of the location of the disease, but confirmation may often be obtained by an abdominal film which may show a distended bowel full of feces and gas above an obviously narrowed segment. If the tumor can be reached by sigmoidoscopy a biopsy can readily be taken by careful curettage, permitting adequate histological examination of the specimen. It is important to mention that, at times, tumors obstructing the rectum or rectosigmoid may arise from structures in the pelvis or may even represent gravity metastases from upper abdominal neoplasms. In this event sigmoidoscopy and radiological studies will merely reveal evidences of pressure external to the lumen of the bowel. A note of warning should be given regarding the danger of radiological examination by means of a barium meal in the presence of obstructing lesions of the colon.

The localization of pain due to neoplasm of the bowels is, in most instances, in the hypogastrium, and this point can be verified by careful history. At times, however, upper abdominal discomfort or pain may be present, particularly if the lesions are near the hepatic or splenic flexures or are in the transverse colon or if extreme distention of the ascending and transverse colon is present because of obstruction at a lower level. This interpretation of the history may lead to the giving of barium by mouth in a search for gastric or small bowel disease. If the narrowing of the colon is marked, serious obstructing symptoms may be precipitated by the giving of a barium meal which may not only complicate the immediate situation but render proper surgical measures difficult and more dangerous. It is essential, therefore, that a very adequate interpretation of the history be obtained before orders are given for radiological studies.

*Treatment.*—The treatment of malignant disease of the large bowel must of necessity be surgical. The results of rectal and colonic surgery for neoplasm are very much better than those obtained following operation for neoplasm of the upper digestive tract. Reports of five year cures suggest that 20 or 30 per cent of the resections are successful. The number of resectable tumors, even when palpable masses are present, is probably better than 50 per cent. Careful preoperative preparation is highly essential, and in right-sided colonic malignancy, treatment of the accompanying anemia is absolutely necessary. It goes without saying that an early diagnosis is desirable. In this connection, it is important to point out that apparently benign polypoid lesions are all too frequently neglected in the hope that they may not undergo malignant degeneration. Such a course is unjustifiable and frequently leads to the development of inoperable cancer.

## ACUTE INFLAMMATORY DISEASE ULCERATIVE COLITIS

Acute inflammatory disease of the colon may be due to infectious agents, as in the case of bacillary dysentery, *Salmonella*, typhoid, and other enteric infections. More chronic forms of ulcerative disease of the colon may be due to specific causes such as tuberculosis, amebiasis and schistosomiasis. These conditions are fully described in other sections. Aside from these disease entities ulcerative colitis may occur as a chronic, progressive disease without known etiology. It is characterized by remissions and relapses in most instances. Typically, it is first encountered in the second and third decades of life, but it may occur in young children or in aged persons. Although primarily a disease of young adults, there is no predominant sex or racial distribution. The onset of the disease is usually insidious, but the condition may be ushered in by an acute attack of fever, nausea and vomiting, and diarrhea. Occasionally, the early symptoms are those of constipation, with the passage of blood and mucus on the outside of formed stools. Although intensive studies have been carried out in an attempt to identify the causative factors, no proof exists that the condition is caused solely, or even usually, by any single infectious agent. Attacks may apparently be precipitated by such diverse conditions as bacillary dysentery, Salmonella infection, measles and episodes of so called intestinal grippe or other virus like diseases. The initial attack may be violent and may

sick individuals oral intake will be entirely inadequate and parenteral feeding necessary but every effort should be made to encourage the patient to take adequate amounts of food by mouth The pain or cramplike discomfort that is frequently associated with active diarrhea may be alleviated by preparations of opium and/or atropine but great care must be observed to avoid overdistention of the bowel by the use of such drugs Except in mild cases the use of bismuth preparations or mixtures of kaolin and vegetable mucin is extremely ineffective The use of chemotherapeutic agents and antibiotics will be attended with varying success No one of the sulfonamides can be used with predictable effect and the same holds true for the newer antibiotics In cases with an elevated temperature striking benefit may be obtained at times with a very adequate dosage of sulfadiazine but generous amounts of fluid must be administered to avoid renal complications If sulfadiazine is effective it may be proper to change subsequently to sulfathalidine or sulfasuxidine for use over *periods of several weeks or even longer* Penicillin is rarely of any value Chloramphenicol has been of benefit in some cases and very occasionally aureomycin has seemed to be helpful The latter drug should be used with caution however because of its tendency to produce nausea vomiting and diarrhea Streptomycin rarely is of benefit In general it can be said that the use of antibacterial agents may at times be an important part of the treatment but they can rarely be depended upon to do more than control immediate urgent situations

Attempts have been made to explain the manifestations of ulcerative colitis on an allergic basis As a primary etiological factor allergic disturbances are undoubtedly of rare and dubious significance Food allergy may exist and this should be taken into account in planning dietary management This is particularly true in the presence of active disease where food allergens may be more readily absorbed through a damaged mucosa with subsequent aggravation of symptoms or skin manifestations At best allergic disturbances are of contributory rather than of primary etiological importance

Because of the manifestations of joint involvement erythema nodosum *etc* it has been logical to attempt to treat patients with ulcerative colitis with ACTH or cortisone Experience with these preparations is still too recent to permit proper evaluation It would appear however that striking temporary remissions may be obtained in cases in which there is relatively superficial involvement of the bowel but marked activity of the disease (as evidenced by bloody diarrhea fever and toxic manifestations) Where marked structural changes have occurred in the colon relatively little or no beneficial effect is to be expected The corticosteroids should be used with great caution but it is highly probable that these or similar drugs may provide a very significant addition to our means of therapy They should never be used unless the patient is under close hospital observation

Mention has already been made of the profound emotional disturbances that are *rather characteristic of the disease This* particular phase of the subject is a highly controversial one but there can be no doubt that carefully planned psychotherapeutic measures when combined with good medical care may be of extraordinary help in getting the disease under control Under no circumstances should the treatment of the patient be carried out without full realization that the individual as well as the disease must be successfully managed It should also be recognized that unskilful psychotherapy may precipitate critical situations with extreme suddenness

One special consideration is worthy of mention namely the question of pregnancy in patients with ulcerative colitis Experience has generally shown that planned pregnancy if the women are really desirous of having children can usually be managed successfully without detriment to the patient or any aggravation of the colitis although the immediate postpartum period must be watched with extreme care On the other hand unexpected and undesired pregnancies in ulcerative-colitis patients are almost always attended by serious exacerbations of the disease

balance and clinical tetany associated with a lowered serum calcium Joint changes may occur during active exacerbations of the disease independently of symptoms referable to the colon Occasionally they precede the development of typical ulcerative colitis They are encountered in at least 10 per cent of the cases and can in no way be distinguished from the manifestations of typical rheumatoid arthritis Any or all of the joints of the body may be involved and the condition may prove particularly intractable unless the underlying chronic disease can be very adequately controlled Skin manifestations in general are of three types Erythema nodosum occurs with relative frequency Pustular lesions involving different skin areas may be noted and may require local surgical drainage A very distressing but rare manifestation is the appearance of large superficial sloughing lesions over the lower extremities with crusting or eschar formation These lesions have the appearance of those due to symbiotic bacterial invasion but positive cultures are never obtained Very occasionally, very serious uveitis or keratitis is encountered Such a complication is a very serious one and closely resembles that occasionally seen in rheumatic infection Enlargement of the liver, due to underlying fatty changes, is not uncommon Degenerative changes in the liver sometimes occur with necrosis of parenchymal cells subsequent fibrosis, and the development of a cirrhotic process Pylephlebitis or multiple liver abscesses are sometimes encountered too Another rare manifestation is bacterial endocarditis due to enteric organisms Renal calculi (uric acid) are occasionally the cause of complicating symptoms Indeed it may be said that, during the course of ulcerative colitis the entire spectrum of many of the most important manifestations of internal medicine may be encountered



Fig 209 —Chronic ulcerative colitis The wall is thick and fibrotic and the mucosa is ulcerated and covered with pseudopolyps (Herbut s Surgical Pathology )

*Treatment* —The successful treatment of ulcerative colitis requires a profound knowledge of the science of medicine and endless patience and watchfulness General supportive measures in the presence of serious diarrhea are always of fundamental importance Rest reassurance and at times sedation are of great help Replacement of fluid electrolytes whole blood and vitamins must be carefully carried out whenever needed Dietary measures require that the food intake be adequate in calories and protein and low in roughage In extremely

sick individuals oral intake will be entirely inadequate and parenteral feeding necessary but every effort should be made to encourage the patient to take adequate amounts of food by mouth The pain or cramplike discomfort that is frequently associated with active diarrhea may be alleviated by preparations of opium and/or atropine, but great care must be observed to avoid overdistention of the bowel by the use of such drugs Except in mild cases the use of bismuth preparations or mixtures of kaolin and vegetable mucin is extremely ineffective The use of chemotherapeutic agents and antibiotics will be attended with varying success No one of the sulfonamides can be used with predictable effect and the same holds true for the newer antibiotics In cases with an elevated temperature striking benefit may be obtained at times with a very adequate dosage of sulfadiazine, but generous amounts of fluid must be administered to avoid renal complications If sulfadiazine is effective it may be proper to change subsequently to sulfathalidine or sulfasuxidine for use over periods of several weeks or even longer Penicillin is rarely of any value Chloramphenicol has been of benefit in some cases and very occasionally aureomycin has seemed to be helpful The latter drug should be used with caution however, because of its tendency to produce nausea vomiting and diarrhea Streptomycin rarely is of benefit In general it can be said that the use of antibacterial agents may, at times be an important part of the treatment but they can rarely be depended upon to do more than control immediate urgent situations

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Surgical interference may be necessary at any time in the course of the disease, either to save life, to render the patient a useful individual, or ultimately to provide a complete cure of the condition. Ileostomy is the only proper initial procedure. In fulminating cases, ileostomy as a life-saving procedure is very disappointing and the risk may be greater than that of conservative treatment. Except for the very acute, violent manifestations of the disease, ileostomy as a life saving procedure usually implies that the physician has waited too long before calling for surgical help. A proper attitude toward ileostomy is as follows: when the patient ceases to be reasonably active because of his disease, ileostomy should be performed as an elective measure. The newer mechanical devices at present available, skilful care of the operative site and the early employment of sealed collecting bags have appreciably reduced the handicaps of ileostomy life. Total colectomy after ileostomy may be indicated and should be performed if diarrhea or bleeding persists or if acute exacerbations of the disease recur. In disease of long standing, either before or after ileostomy, the danger of carcinomatous change in the colon should not be overlooked. The incidence of cancer in chronic cases of this disease is undoubtedly higher than in the general population, and the careful physician should constantly bear this in mind in planning adequate supervision of his patient. An additional indication for ileostomy is the presence of intractable perianal sepsis, recto-vaginal fistulæ, eye complications or crippling joint manifestations. Acute perforation of the bowel obviously demands surgical intervention.

# DISEASES OF THE LIVER

## GENERAL CONSIDERATIONS

An adequate understanding of hepatic disease must include a reasonable knowledge of liver anatomy and function. Structurally the liver is composed of parenchymal (polygonal) cells, reticulo-endothelial cells (Kupffer cells), sinusoids, biliary canaliculi and ducts, stroma, and vascular elements. Hepatic disease may involve primarily any of these anatomical structures. Thus toxic or infectious agents may damage the parenchymal cells, thereby interfering with anabolic and catabolic processes essential to the body economy. External interference *with the ductal system may produce back* pressure into the bile canaliculi, with resulting bile stasis and cholangitis. Generalized disease of the reticuloendothelial system may involve these elements in the liver, or they may be affected directly by infectious agents or particulate matter. Disease of the portal system or trauma to the hepatic artery or its radicles may reduce the blood supply of the liver to an important degree. Congestive heart failure or pressure on the hepatic veins may prevent adequate venous return from the organ, with resulting venous stasis, swelling and tissue anoxia. In the early stages of any given disease any one of these elements may be solely affected. As the disease process progresses, all the structural elements may become involved, either in a diffuse necrotizing process or in the changes that accompany repair and scar tissue formation. On the basis of our present knowledge it is not possible to state that serious damage to the reticulo-endothelial system is necessarily fatal. Extensive damage to the parenchymal cells with destruction of a large number of these functional elements will invariably result in varying degrees of hepatic failure, which may lead to coma and a fatal outcome. Any consideration of the results of damage to the liver should include a thorough realization of the fact that the organ possesses tremendous powers of repair in the face of extensive damage. Indeed it can be said that immediate survival after serious liver injury will depend upon the adequacy of the repair process in relation to the amount of parenchymal tissue destroyed, regardless of architectural changes. In the more chronic forms of liver disease *compensation to structural damage* will depend upon the degree of regeneration of functional elements. The ultimate prognosis and the degree of useful activity that may be acquired in the presence of permanent liver damage will eventually depend upon the actual mass of functioning parenchymal cells. Therapy, therefore, *must be* continuously directed toward those measures

which spare the liver encourage cellular regeneration and replace temporarily or permanently damaged hepatic functions

The functions of the liver are numerous and by no means thoroughly understood In general they can be grouped under three headings (1) excretory (2) metabolic, and (3) detoxifying or bacteriocidal Normal excretory function may be said to involve the elimination or passage of such substances as bilirubin bile acids alkaline phosphatase foreign substances such as aniline dyes and cholesterol Metabolic processes include gluconeogenesis glycolysis deamination of amino acids and other aspects of protein *metabolism phospholipid metabolism* fat transport fibrinogen formation prothrombin formation the formation of vitamin A from carotene and numerous other intricate biochemical processes The liver is the sole source of bile acids and one of its most important functions is the maintenance of optimum levels of albumin in the blood In addition to the formation of fibrinogen hepatic function undoubtedly includes an active participation in the combining of heme and globin It also contributes a factor necessary for the proper maturation of the red cells The parenchymal cells and the reticulo-endothelial cells are undoubtedly concerned with bacteriolysis and immunological processes and the detoxification or conjugation of various poisonous substances such as belladonna alkaloids morphine and the like In some imperfectly understood fashion the liver also is undoubtedly concerned with the conjugation of steroids and hepatic failure is at times accompanied by clinical manifestations of estrogen or androgen imbalance

Attempts to measure abnormalities in any of the above mentioned hepatic functions are only partially successful In many instances quantitative deviations from normal behavior may be demonstrated In others only qualitative changes may be shown Of some aspects of liver function our knowledge is still so vague as to enable u merely to guess at the nature and the degree of the underlying disturbance At best liver function tests must represent imperfect and rather crude attempts to estimate functional abnormalities It should never be forgotten that a very large degree of damage must be present before any of the tests measuring hepatic function show evidences of abnormal behavior This is particularly true in relation to those tests which attempt to measure parenchymal-cell function In the clinical use of liver function tests it is to be emphasized that the results of such examination are not usually diagnostic although they occasionally give reasonably exact information For the most part diagnoses are made on the basis of clinical skill and confirmation is obtained by laboratory measures On the other hand it is also important to recognize that the progress of *a given disease of the liver may be followed* with much greater accuracy by the careful use of selected tests of liver function than in any other manner

Specific liver function tests warrant brief and somewhat general consideration The detailed techniques of individual tests will be found in original articles Tests of excretory function include simple examination of the urine and stools for the presence or absence of bile pigments Thus in cases of obstructive lesions the urine will contain excessive amounts of bilirubin and the stools will contain little or none of this pigment depending upon the degree of obstruction Where obstruction is great stool and urinary urobilinogen will be markedly diminished In complete obstruction of the external biliary passages the stool will be completely clay-colored and will contain no bilirubin or urobilinogen (except in rare instances) and the urine will be free of urobilinogen Typically in cases of obstruction, the blood serum contains increased amounts of bilirubin and at the same time yields high values for alkaline phosphatase and in many instances total cholesterol The highest values of alkaline phosphatase and cholesterol in the serum will be encountered in cases of complete obstruction due to neoplasm or in those unusual cases of cholangiolitis with a high degree of intracanalicular block Any degree of biliary obstruction either internal or external will show increased retention of bromsulphalein in the blood serum Exclusion of bile from the duodenum results in a short time in faulty absorption of fat-soluble vitamin K with hypoprothrombinemia

Surgical interference may be necessary at any time in the course of the disease either to save life, to render the patient a useful individual, or ultimately to provide a complete cure of the condition Ileostomy is the only proper initial procedure In fulminating cases, ileostomy is a life saving procedure is very disappointing and the risk may be greater than that of conservative treatment Except for the very acute violent manifestations of the disease ileostomy as a life-saving procedure usually implies that the physician has waited too long before calling for surgical help A proper attitude toward ileostomy is as follows when the patient ceases to be reasonably active because of his disease, ileostomy should be performed as an elective measure The newer mechanical devices at present available, skilful care of the operative site and the early employment of sealed collecting bags have appreciably reduced the handicaps of ileostomy life Total colectomy after ileostomy may be indicated and should be performed if diarrhea or bleeding persists or if acute exacerbations of the disease recur In disease of long standing either before or after ileostomy the danger of carcinomatous change in the colon should not be overlooked The incidence of cancer in chronic cases of this disease is undoubtedly higher than in the general population and the careful physician should constantly bear this in mind in planning adequate supervision of his patient An additional indication for ileostomy is the presence of intractable perianal sepsis recto vaginal fistulæ eye complications or crippling joint manifestations Acute perforation of the bowel obviously demands surgical intervention

# DISEASES OF THE LIVER

## GENERAL CONSIDERATIONS

An adequate understanding of hepatic disease must include a reasonable knowledge of liver anatomy and *function* Structurally the liver is composed of parenchymal (polygonal) cells, reticulo-endothelial cells (Kupffer cells), sinusoids biliary canaliculi and ducts stroma, and vascular elements Hepatic disease may involve primarily any of these anatomical structures Thus toxic or infectious agents may damage the parenchymal cells, thereby interfering with anabolic and catabolic processes essential to the body economy External interference with the ductal system may produce back pressure into the bile canaliculi, with resulting bile stasis and cholangitis Generalized disease of the reticuloendothelial system may involve these elements in the liver, or they may be affected directly by infectious agents or particulate matter Disease of the portal system or trauma to the hepatic artery or its radicles may reduce the blood supply of the liver to an important degree Congestive heart failure or pressure on the hepatic veins may prevent adequate venous return from the organ with resulting venous stasis, swelling and tissue anoxia In the early stages of any given disease any one of these elements may be solely affected As the disease process progresses, all the structural elements may become involved either in a diffuse necrotizing process or in the changes that accompany repair and scar tissue formation On the basis of our present knowledge, it is not possible to state that serious damage to the reticulo endothelial system is necessarily fatal Extensive damage to the parenchymal cells with destruction of a large number of these functional elements will invariably result in varying degrees of hepatic failure which may lead to coma and a fatal outcome Any consideration of the results of damage to the liver should include *a thorough realization of the fact that the* organ possesses tremendous powers of repair in the face of extensive damage Indeed it can be said that immediate survival after serious liver injury will depend upon the adequacy of the repair process in relation to the amount of parenchymal tissue destroyed regardless of architectural changes In the more chronic forms of liver disease compensation to structural damage will depend upon the degree of regeneration of functional elements The ultimate prognosis and the degree of useful activity that may be acquired in the presence of permanent liver damage will eventually depend upon the actual mass of functioning parenchymal cells Therapy therefore must be continuously directed toward those measures

Two other diagnostic measures should be mentioned first punch biopsy of the liver which has now been employed over a sufficient number of years to justify its occasional use both as a means of establishing a definite diagnosis and as a means of determining the probable stage or phase of the disease under consideration secondly radiological examination of the esophagus which is important in order to demonstrate the presence of esophageal varices as the cause of actual or potential bleeding in the presence of chronic liver disease

The *diagnosis* of liver disease in general will depend upon an adequate history, with full details as to exposure to infectious or toxic agents dietary habits and the duration and nature of individual symptoms Physical examination may yield little information but as a rule provides clear evidence of involvement of some part of the biliary system Icterus of the scleræ and skin enlargement of the liver and spleen the presence of a collateral circulation spider angiomata xanthomata and so-called liver palms give clear indication of hepatic disorder which may be primary or secondary to other serious disease Further evidence as to the severity of the underlying liver disease may be suggested by the finding of ascites and/or peripheral edema purpuric manifestations and the presence of a rather distinctive odor to the breath known as fetor hepatis In most instances a careful history and an equally careful physical examination will provide clear evidence that liver disease is present and frequently will indicate the essential nature of the process Information obtained by means of laboratory tests in most instances will be confirmatory of already established working diagnoses In other instances a definitive diagnosis will be impossible until the patient has been followed for an appreciable period of time or until surgical exploration has provided the final necessary information This last point is of extreme importance inasmuch as certain types of jaundice are extremely baffling and prolonged waiting for a final diagnosis may permit the occurrence of progressive hepatic failure to a point where proper surgical measures are ineffective because of the critical condition of the patient

*Treatment* —The general principles underlying the treatment of liver disease are clear In the presence of external biliary obstruction surgical relief of obstruction is essential and other measures will be of little or no value except in diminishing surgical risks In non-obstructive cases rest is important in order to reduce to a minimum the metabolic requirements of the individual At the same time, there must be adequate provision of nutrient material either orally or parenterally to spare the breakdown of body protein and to meet the tissue requirements necessary for the maintenance of metabolic processes and the repair of damage Thus a diet adequate in calories and relatively generous in protein is an essential therapeutic consideration Vitamin requirements may be met by properly balancing the diet or by the administration of specific substances as needed Noxious agents that may have been responsible for the liver damage must be eliminated and drugs or other specific substances that might further harm the liver must be avoided Specific infection must be controlled either by adequate surgical drainage of the biliary tract if an obstructive process is present or by the use of suitable antibiotics Transfusions will serve to replace blood that has been lost through hemorrhage or temporarily raise hemoglobin levels where hematopoiesis is diminished In rare instances low serum albumin levels may be temporarily raised with benefit to the patient by the intravenous use of human serum albumin Because of the frequent occurrence of pain and restlessness analgesics or sedatives may be needed Morphine and opium derivatives should be used with extreme caution in the presence of a sick liver inasmuch as they are conjugated slowly and rather inadequately with the result that an ordinary dose may become an overdose The same caution should be observed in the use of the barbiturates Control of fluid and electrolyte balances will be treated in the discussion of specific manifestations of liver disease Ascites and peripheral edema may require the use of a low sodium diet mercurial diuretics and under proper circumstances the employment of ion-exchange resins

Brief consideration should be given to the differentiation of various types of hyperbilirubinemia. In hemolytic jaundice of any type in which there is an excessive amount of bilirubin in the serum resulting from abnormal breakdown of red blood cells, there is an absence of prompt direct reacting bile pigment and of bilirubinuria (acholuric jaundice). Such a finding in the serum is also to be noted in the jaundice encountered in instances of icterus neonatorum and in so-called constitutional hepatic dysfunction, in which only an indirect van den Bergh reaction is found. In disease conditions affecting primarily the integrity of the liver parenchyma or in frank biliary obstruction total serum bilirubin will consist of two components measured by the van den Bergh test (1) prompt, direct reacting serum bilirubin (one-minute bilirubin) and (2) total bilirubin (indirect-reacting bilirubin). The relationship between the prompt-reacting fraction and total bilirubin has little definitive diagnostic importance, although high values for the prompt reacting fraction are most frequently found in cases of uncomplicated extrahepatic obstruction.

Tests of metabolic functions of the liver are numerous and varied. In the absence of jaundice, the most delicate test of impaired parenchymal-cell function is that obtained by the administration of bromsulphalein by vein (5 mgm. per kilogram of estimated body weight) and the determination of the amount of dye retained in the blood serum at the end of 45 minutes. Acute severe liver damage usually results in an alteration of the albumin globulin fractions of the blood plasma. The cephalin-cholesterol flocculation and thymol turbidity and flocculation are positive and the gamma globulin concentration in the serum is high. In the very acute, severe manifestations of hepatic disorders or in the more chronic forms there is a tendency to a steady diminution in the level of serum albumin and an associated rise in the globulin values particularly that of gamma globulin. The total serum protein may fall below normal levels but, more frequently, is essentially normal with an inversion of the albumin globulin ratio. Determination of this ratio *per se* yields little prognostic or therapeutic information but the actual level of serum albumin gives significant information of the functional capacity of the liver in the absence of recent bleeding. The demonstration of hypoprothrombinemia may indicate merely interference with proper excretion of bile into the intestinal tract. A diminished plasma prothrombin may also provide a very adequate indication of parenchymal-cell damage, and this will be readily confirmed by failure to rectify this abnormality following the administration parenterally of vitamin K. Less satisfactory tests of impairment of certain metabolic functions of the liver are to be obtained by the use of the galactose-tolerance test and hippuric acid test, and the determination of the ratio between cholesterol esters and total serum cholesterol. Measurement of urobilinogen in the urine in the absence of any degree of external biliary-tract obstruction, provides a relatively simple means of estimating parenchymal cell damage. Increased urinary values nearly always signify rather extensive damage and a return toward normal levels in the absence of increasing obstruction provides a favorable prognostic sign.

The selection of any of these tests, in most instances should be based upon a careful clinical evaluation of the individual case. At times the whole "battery" of tests is necessary in order to obtain adequate diagnostic help. In most instances however a working diagnosis will enable the physician to choose a small number of tests to be employed in order to gain confirmatory evidence as to the nature of the underlying condition without undue loss of time or unnecessary expense to the patient. It should be remembered that no single test is diagnostic and that even in classical cases of certain forms of liver disease certain tests may be temporarily quite misleading. Thus in parenchymal disease of the liver one or more of the flocculation tests occasionally may be entirely negative. Similarly in minor degrees of jaundice bromsulphalein retention may unexpectedly fall within normal limits. In any given case it is important to choose those tests the results of which are positive and then follow these consistently in order to determine the progress and trends of the disease process.

disease Pertinent laboratory procedures will include examination of the urine and the stools As a rule, the stools will show a moderate or normal amount of bile pigment on gross examination The urine will contain not only bilirubin but excessive amounts of urobilinogen The results of flocculation tests may be definitely positive and the cholesterol esters will usually be found to be definitely diminished In severe cases leukocytosis will be present indicating a severe degree of necrosis

*Treatment* obviously must include removal of the noxious agent particularly if this is a recently administered drug Absolute rest is necessary and an adequate amount of fluid and a well balanced diet are essential In the milder cases these two measures can be provided without difficulty In cases in which anorexia nausea and vomiting exist feeding may be difficult and parenteral therapy may be necessary In moderately severe cases small amounts of simple food may be tolerated and the remainder may be supplied by vein in the form of dextrose solutions in saline or in water depending upon the amount of vomiting that has taken place At times the use of constant feeding through a nasal catheter may make it possible to meet dietary requirements in cases in which nausea interferes with proper oral feeding Under such circumstances the use of milk powder Karo or banana powder and moderate amounts of Brewers yeast may provide a satisfactory mixture Where severe liver damage has occurred it may be wise to use concentrated solutions of dextrose (25 per cent solution) in order to meet caloric requirements spare the breakdown of body protein and obviate the administration of excessive quantities of fluid The use of lipotropic substances such as methionine or choline probably offers little if adequate nutrient material can be given by mouth Where this is impossible one of these agents may be given parenterally in the hope that it may prove of some benefit The use of vitamin B concentrates is usually advocated but there is little evidence that they contribute much to effective therapy If the patient tolerates a good diet they are not needed If ingestion of food is limited vitamin preparations may be given by vein but it should be remembered that niacin amide may not be utilized by a sick liver and may compete for methyl groups which might otherwise be utilized in the natural formation of choline from methionine-containing substances If sedation is necessary because of restlessness muscular tremor or convulsions it is wise to avoid the use of the barbiturates and to employ safer preparations such as chloral hydrate or paraldehyde Morphine or opium derivatives or synthetic substances such as demerol or methedon should be used with great caution if necessary to control abdominal pain Where it is obvious that the liver is severely damaged these preparations are probably contraindicated

*Prognosis* —As noted above the prognosis in toxic damage to the liver will depend upon the dosage of the specific poison the length of the exposure and the susceptibility of the patient If there is coexisting malnutrition chronic alcoholism diarrhea or any other debilitating condition the outlook may be extremely grave and the need for replacement therapy immediate Once the diagnosis of intrahepatic damage is made regardless of the underlying cause continuous intensive treatment is necessary until the patient shows striking signs of improvement The term *acute yellow atrophy* already alluded to does not represent a specific disease entity It merely is an indication of a severe necrotizing destructive process that may occur in the presence of any form of liver injury that is extensive and progressive The greater the degree of atrophy the greater the degree of liver insufficiency and the worse the prognosis

VIRAL HEPATITIS (ACUTE CATARRHAL JAUNDICE EPIDEMIC INFECTIOUS JAUNDICE SERUM HEPATITIS) —Under this heading should be included what for many years was classified as acute catarrhal jaundice For therapeutic purposes epidemic infectious hepatitis and serum hepatitis can be grouped together as representing serious diffuse infection of the liver probably by specific viruses Clinically the two conditions should be differentiated because of differences in the manner in which the disease is acquired in the incubation period and in immune responses Either of these two

## SPECIFIC DISEASES OF THE LIVER

*The diseases of the liver may be roughly* classified into acute and chronic They may be further divided into conditions due to specific agents toxic to the liver or specific infections of the liver conditions associated with degenerative changes, disorders due to obstruction either in the external biliary ducts or in the bile canaliculi and finally infiltrating neoplasms

TOXIC HEPATITIS —Acute damage to the liver may result from a variety of known agents Among these are certain chemicals such as chloroform, carbon tetrachloride trichlorethylene, tetrachlorethane, trinitro toluol, phosphorus tannic acid, beryllium arsenic cincophen and many other sub stances All these agents cause diffuse hepatic damage with necrosis of parenchymal cells In most instances the toxic agents produce rather acute hepatic damage with rapidly progressing symptoms of liver insufficiency In the case of beryllium and certain inorganic arsenic compounds the process may develop much more slowly The lesions produced in the liver by these various agents vary considerably Thus beryllium poisoning produces diffuse gran ulomatous change in the organ and is rarely associated with acute hepatic insufficiency Arsphenamine and cincophen for example involve the entire hepatic lobule Central necrosis is caused by chloroform carbon tetrachloride, and the like The lesions due to phosphorus primarily *involve the periphery* of the lobule In spite of histological differences liver damage due to noxious agents such as those noted above is a diffuse process, which involves the entire organ and is accompanied by varying degrees of parenchymal-cell destruction and loss of primary hepatic functions The degree of damage will depend upon the dose of the poisonous substance the duration of exposure and the susceptibility of the individual patient In any event, the clinical manifestations of this type of insult to the liver produce hepatic insufficiency, which in extreme cases may progress to a fatal outcome because of the destruction of a sufficient number of paren chymal cells In most instances, jaundice is the presenting clinical feature Loss of appetite nausea, and vomiting are com monly encountered and may steadily in crease in severity Where only mild intoxi cation is present, physical signs in addition to icterus may reveal moderate hepatic enlargement, with local tenderness In the more severe cases jaundice will be more intense and hepatic enlargement and tender ness will at first be more striking If a great deal of damage has been produced, necrosis of the liver may progress in spite of attempts at repair, until real hepatic failure is present At this point, the picture of acute yellow atrophy may be present with a gradual diminution in size of the liver and the devel opment of abdominal distention, which is in the nature of a paralytic ileus Ascites may occur The patient will become restless muscular movements may become jerky or convulsive and finally, drowsiness and coma may supervene A heavy mousy odor may be noted on the breath at any stage of the condition and is usually evidence of pro found liver damage A point of clinical importance is that patients with diffuse damage to the liver parenchyma, on the basis either of toxic agents or of infection may apparently be progressing favorably and then almost without warning deteriorate rapidly and slip into a terminal coma Among important prognostic features should be noted increasing oliguria and a steady rise in pulse rate and in temperature A progres sively diminishing urinary output is always a bad prognostic sign Conversely, a stead *ily increasing urinary output except as a* rare terminal event indicates a favorable response to therapy

*Diagnosis* —The diagnosis will usually be apparent from the physical signs noted above together with a history which will indicate exposure to a toxic agent and a story of recent and rapidly developing symptoms At times initial diagnosis may be difficult because of the fact that the patient may complain of right upper-quadrant pain which with the local tenderness and jaun dice may suggest the possibility of a stone in the common duct or acute cholecystitis The degree of prostration and the diffuse tenderness to palpation or compression of the liver will be points in favor of intrahepatic

persists until the disease abates Itching is a variable feature, which may be so extreme as to produce intense scratching with excoriation of the skin and sometimes, superficial skin infection In fulminating cases or cases in which there is extreme progressive derangement of liver function striking atrophy of the liver may occur, with demonstrable reduction in size and the concomitant signs of hepatic failure previously described

*Diagnostic Measures* —The diagnosis is usually easily made on the basis of history and physical findings In most instances laboratory studies reveal varying grades of hyperbilirubinemia and the presence of bilirubin in abnormal amounts in the urine, and in diminished quantities in the stools Urinary urobilinogen at first is increased but subsequently may fall to normal or subnormal levels again rising however, during the recovery period to high levels before eventually returning to normal In the most severe cases albuminuria is a constant finding together with the appearance of cellular elements and casts Before intense jaundice has appeared, the bromsulphalein test may be one of the first to show striking abnormalities Subsequently flocculation tests will become positive and will usually remain so during the active course of the disease Alkaline phosphatase and cholesterol levels may be moderately elevated, and on occasion alkaline phosphatase values in the serum may reach very high levels due to intracanalicular block Prothrombin values are usually reduced depending upon the severity of the disease The level of cholesterol esters is nearly always lowered In the pre icteric stage of the disease a transient leukocytosis may occur Subsequently however the white blood count is usually below normal and may reach very low levels with an absolute reduction in the number of circulating granulocytes Monocytic cells will be relatively or actually increased typically they assume rather bizarre forms forms at times difficult to differentiate from those encountered in infectious mononucleosis These blood changes have been fully described by Jones and Minot In cases of moderate or greater severity erythrocyte levels will drop and the red-cell count may go as low as 2 million red blood cells per cubic millimeter The sedimentation rate at first is normal but gradually becomes accelerated and may be the last laboratory finding to remain positive as evidence of active disease If diagnosis is extremely difficult aspiration biopsy of the liver invariably shows a characteristic histological picture

Radiological studies are chiefly of value in excluding other causes of jaundice although they may occasionally provide diagnostic help by demonstrating an otherwise unsuspected splenic enlargement In certain rare instances examination by barium meal may reveal distortions of the mucosal pattern of the duodenum which are distinguished with difficulty from those due to cancer of the head of the pancreas or the ampulla These changes may be due to frank duodenitis or to pressure on the duodenum by enlarged periductal glands When noted, they should always suggest the possibility of a malignant process, but the presence of laboratory findings entirely consistent with intrahepatic disease rather than typical of external block may make it reasonable to disregard such a possibility

*Course* —In the average case the course of the disease covers a period of from two to four weeks In severe cases it may last for weeks or months and cause marked loss of weight and strength Convalescence is slow, and recovery of strength very gradual The prolongation of the disease over eight or ten weeks indicates a possible change from an acute condition to a continuing, progressive, subacute process Subacute hepatitis eventually leading to so-called post atrophic cirrhosis is fortunately uncommon In fulminating cases, death may occur in from three to five days The disease may apparently progress favorably for several weeks and then suddenly show evidences of greater degrees of liver destruction with an abrupt fatal termination The mortality rate for infectious hepatitis of the epidemic variety is probably no greater than 2 or 3 per cent

*Treatment* —The general principles of rest and the provision of an adequate amount of nutrient material constitute the chief therapeutic measures In the acute stage of the disease it is important that the patient be kept at full rest In the recovery period,

conditions may occur at practically any age They may be encountered sporadically or, in the case of epidemic infectious hepatitis, in true epidemics Serum hepatitis may occur in large groups of individuals and this was the case during World War II, when a specific infectious agent was transmitted by inoculation to large groups of individuals The etiological agent responsible for either type of hepatitis has not yet been fully identified but the work of Stokes, Havens, Neefe, and others presents very convincing evidence of a viral origin for these maladies Stokes and his collaborators have recently cultivated an ultra-filterable agent which may prove to be the cause of the epidemic form of the infection, and skin tests based on this finding are probably of diagnostic significance

### *Epidemic Infectious Hepatitis*

This condition is due to an agent that can be transmitted to human beings by material obtained from stools of patients with the disease Therefore it is presumably transmitted by flies and other insects and by human carriers who pollute food and other ingesta Fecal contamination of water has been shown to be a source of epidemics Inhalation of infectious material probably does not cause the disease, except in rare instances It is also doubtful whether the disease is transmitted by means of inoculation with infected instruments or solutions The average incubation period of the disease is approximately three weeks but may vary from two to six weeks

The *histological changes* taking place in the liver in this disease consist characteristically of necrosis of the parenchymal cells of greater or less degree sometimes involving individual cells, sometimes involving wide areas of hepatic tissue Cellular infiltration occurs in these areas Ordinary regeneration of parenchymal damage is complete and leaves little or no evidence of the disease but, in the fulminating cases, evidences of regeneration are minimal, and almost complete autolysis of the liver may occur In subacute cases regeneration occurs in an irregular fashion, with complete change in the liver architecture, due to fibrosis and *condensation of hepatic units* Eventually, the process may go on to the full blown picture of cirrhosis

The onset of *symptoms* is characteristically abrupt and may be ushered in by chills and fever Nausea and vomiting with marked loss of appetite and a distaste for food are quite characteristic, diarrhea may occur In some instances symptoms occur so gradually as to be unnoticed for days, but in almost every instance there is eventually a lack of desire for food and nausea if not frank vomiting Abdominal pain may occur as an early symptom and may be sufficiently severe to suggest the possibility of cholelithiasis or cholecystitis, particularly if jaundice is present Usually, within from ten days to two weeks of the initial symptoms, scleral icterus and the appearance of dark urine and light-colored stools are noted The disease may occur however, without ever showing clinical icterus or even hyperbilirubinemia a fact of clinical significance inasmuch as the correct diagnosis may be missed completely and inadequate therapy may be instituted In the vast majority of cases, fever is not present once clinical icterus is noted a point of importance in differentiating virus hepatitis from conditions such as cholelithiasis, cholangitis, pylephlebitis multiple liver abscesses *etc*

On *physical examination* the most important sign is that of a slightly enlarged liver, which is tender to palpation or compression Icterus is usually present and may become intense in the course of a few days or may remain at a very minimal level Slight enlargement of the spleen should be looked for as confirmatory evidence of liver disease, and with care can be demonstrated by palpation or percussion in possibly half of the cases Demonstration of splenic enlargement is of particular importance in differentiating cases of infectious hepatitis from jaundice secondary to occlusion of the common duct in which splenomegaly is not to be expected Generalized lymphadenopathy may occasionally be encountered In severe cases abdominal distention ascites and peripheral edema may occur and occasionally spider angiomata are observed One characteristic phenomenon is the frequent association with mental depression which

cent have been reported Diagnostic and therapeutic measures differ in no way from those discussed in the preceding section One point of clinical importance lies in the fact that so-called serum hepatitis particularly that occurring sporadically frequently follows perfectly proper surgical procedures The appearance of jaundice a few months after upper abdominal surgery may erroneously be considered a complication of the surgical procedure and result in an exploratory laparotomy Such a decision is extremely unfortunate and may result in a fatal outcome if the jaundice is due to intrahepatic infection Therefore it is of extreme importance in postoperative patients to determine the period of time elapsing between the operation and the appearance of icterus inasmuch as this may give the first clue as to the underlying condition Confirmatory and suggestive evidence may further be found in the fact that the patient has received a number of whole-blood transfusions or still more important one or more units of plasma When these facts can be elicited it is essential that all the findings be carefully evaluated with the aid of appropriate liver function tests in order to avoid unnecessary and dangerous surgery

*Prevention* —Whenever possible all instruments that might carry the infectious agent such as solid and hollow needles scalpels *etc* should be carefully autoclaved before use and not used again until further similar sterilization has been provided Transfusions with whole blood should not be provided from donors who have had jaundice within the preceding three months The use of plasma should be limited to emergencies and as far as possible plasma units should be derived from the smallest possible pools Human fibrin preparations should be used with great caution and should indeed be avoided unless products of animal origin are unobtainable Partial sterilization of plasma may be obtained through ultraviolet irradiation and possibly through the use of nitrogen mustard Neither of these measures however affords full protection against contamination As in the epidemic form one attack of the disease almost always protects against further infection The use of gamma globulin probably has no value as a prophylactic measure

Other Acute Hepatic Infections — Among other infections primarily affecting the liver mention should be made of such conditions as yellow fever spirochetosis ictero-hemorrhagica infectious mononucleosis typhoid and parasitic infestations such as amebiasis and schistosomiasis These disease entities are fully covered in other sections However brief mention should be made of *infectious mononucleosis* This condition occasionally closely simulates infectious hepatitis Differential points in the diagnosis are the more generalized adenopathy and the greater enlargement of the spleen that are usually encountered in infectious mononucleosis as well as the positive heterophile agglutination usually present after the initial stages of the disease and the characteristic changes in circulating leukocytes In infectious mononucleosis leukocytosis is common and leukopenia rare In most of the cases the appearance of monocytes is diagnostic

*Acute biliary obstruction* is practically always the result of interference with the normal flow of bile through the external biliary passages into the duodenum by biliary calculi new growth postoperative trauma to the common duct or the pressure on the common duct of enlarged glands due to infectious disease It may also occur as the result of a congenital anomaly atresia of the common bile duct Unless accompanied by serious infection of the biliary radicles proximal to the level of obstruction little actual damage to the liver results When obstruction persists for any period of time back pressure occurs with dilatation of the biliary radicles and infection by coliform or or other enteric organisms When uncorrected there may be eventual deterioration of hepatocellular function with resulting hepatic insufficiency The condition is essentially a surgical one and adequate drainage measures are always indicated with appropriate added measures to control any infection that is present Postponement of surgical intervention except where obstruction is due solely to the enlargement of lymph glands in the course of infectious disease or is a manifestation of metastatic

moderate exercise should be permitted but should always be kept below fatigue levels. The use of alcohol during or immediately after attacks of hepatitis should be prohibited, as should the use of medications that are known to be hepatotoxic agents. The point at which full activity should be allowed is not always easy to determine, but in general it can be stated that too early ambulation with associated physical fatigue may produce relapses, with at times sudden painful enlargement of the liver and an increase in jaundice. The persistence of a rapid sedimentation rate, positive results in flocculation tests, abnormal bromsulphalein retention, or definite hypoprothrombinemia should warrant continued conservative treatment. A slightly elevated serum bilirubin *does not necessarily indicate* continued activity of the process. In fulminating or very severe cases therapy must be pushed continuously in the hope of saving life or of protecting the liver from irreparable damage. In cases in which a subacute or chronic process evolves, a carefully planned program of therapeutic measures and of regulated activity must be outlined. The use of antibiotics in the acute stages of the disease has proved to be of no value whatever. At the present time limited studies suggest that the course of the disease may be shortened appreciably by the use of corticosteroids but, to date, the evidence is not conclusive and ultimate decision as to this form of therapy must wait for further careful clinical investigation.

*Prophylactic measures* are of importance in order to prevent the spread of the epidemic form of the disease. Personnel caring for individuals ill with epidemic infectious hepatitis should be extremely careful to wash their hands carefully after handling the patient. Bed linen and fomites should be treated with infectious precautions. In institutions or in groups of individuals among whom the disease appears an important degree of protection for exposed persons may be obtained by the use of gamma globulin which contains immune bodies.

*Immunity*.—In most instances a single attack of the disease confers a lasting immunity, but recurrences after long intervals have been reported. It is extremely important to note that this disease does not confer immunity to infection by the agent responsible for serum hepatitis, and the converse is equally true.

### Serum Hepatitis

Serum hepatitis is quite similar to the entity described above in that it represents an acute diffuse infectious process involving the liver parenchyma, with varying degrees of liver damage and insufficiency. Certain important characteristics should be noted. This disease is acquired in almost every *instance by the introduction of the* infectious agent through the skin. Transmission by ingestion or inhalation probably does not occur, or only on rare occasions. The agent may be introduced by venipuncture needles contaminated from other individuals harboring the disease and by the use of infected whole blood, plasma, or other blood products such as human fibrin. It may be transmitted as a laboratory accident from contaminated instruments or containers. After inoculation of infected material in the course of group immunization to specific disease the most common source of infection is in the therapeutic use of whole blood or its fractions. The use of plasma is more dangerous than that of whole blood inasmuch as plasma is usually derived from a fairly large pool of donors, any one of whom may contribute the infectious agent. Commercially prepared fibrin for use in surgical operations constitutes another serious source of the disease if the fibrin product is of human origin. As far as the danger arising from contaminated instruments and containers is concerned, full protection can be obtained only by sterilization under autoclave conditions.

The incubation period of the disease, unlike that of epidemic infectious hepatitis, averages about three months; it may vary from two to possibly six months. The onset and the subsequent course of the disease are essentially the same as the onset and the course of the epidemic form of hepatitis but available statistical evidence would indicate that the condition carries a higher mortality rate than the epidemic form. Mortality rates as high as from 10 to 14 per

cent have been reported. Diagnostic and therapeutic measures differ in no way from those discussed in the preceding section. One point of clinical importance lies in the fact that so-called serum hepatitis, particularly that occurring sporadically, frequently follows perfectly proper surgical procedures. The appearance of jaundice a few months after upper abdominal surgery may erroneously be considered a complication of the surgical procedure and result in an exploratory laparotomy. Such a decision is extremely unfortunate and may result in a fatal outcome if the jaundice is due to intrahepatic infection. Therefore it is of extreme importance in postoperative patients to determine the period of time elapsing between the operation and the appearance of icterus, inasmuch as this may give the first clue as to the underlying condition. Confirmatory and suggestive evidence may further be found in the fact that the patient has received a number of whole blood transfusions or, still more important, one or more units of plasma. When these facts can be elicited it is essential that all the findings be carefully evaluated with the aid of appropriate liver function tests in order to avoid unnecessary and dangerous surgery.

*Prevention.*—Whenever possible all instruments that might carry the infectious agent, such as solid and hollow needles, scalpels, *etc.*, should be carefully autoclaved before use and not used again until further similar sterilization has been provided. Transfusions with whole blood should not be provided from donors who have had jaundice within the preceding three months. The use of plasma should be limited to emergencies and, as far as possible, plasma units should be derived from the smallest possible pools. Human fibrin preparations should be used with great caution and should indeed be avoided unless products of animal origin are unobtainable. Partial sterilization of plasma may be obtained through ultraviolet irradiation and possibly through the use of nitrogen mustard. Neither of these measures, however, affords full protection against contamination. As in the epidemic form, one attack of the disease almost always protects against further infection. The use of gamma globulin probably has no value as a prophylactic measure.

Other Acute Hepatic Infections.—Among other infections primarily affecting the liver, mention should be made of such conditions as yellow fever, spirochetosis ictero-hemorrhagica, infectious mononucleosis, typhoid, and parasitic infestations such as amebiasis and schistosomiasis. These disease entities are fully covered in other sections. However, brief mention should be made of *infectious mononucleosis*. This condition occasionally closely simulates infectious hepatitis. Differential points in the diagnosis are the more generalized adenopathy and the greater enlargement of the spleen that are usually encountered in infectious mononucleosis, as well as the positive heterophile agglutination usually present after the initial stages of the disease and the characteristic changes in circulating leukocytes. In infectious mononucleosis leukocytosis is common and leukopenia rare. In most of the cases the appearance of monocytes is diagnostic.

*Acute biliary obstruction* is practically always the result of interference with the normal flow of bile through the external biliary passages into the duodenum by biliary calculi, new growth, postoperative trauma to the common duct, or the pressure on the common duct of enlarged glands due to infectious disease. It may also occur as the result of a congenital anomaly, atresia of the common bile duct. Unless accompanied by serious infection of the biliary radicles proximal to the level of obstruction, little actual damage to the liver results. When obstruction persists for any period of time back pressure occurs with dilatation of the biliary radicles and infection by coliform or or other enteric organisms. When uncorrected there may be eventual deterioration of hepatocellular function with resulting hepatic insufficiency. The condition is essentially a surgical one and adequate drainage measures are always indicated with appropriate added measures to control any infection that is present. Postponement of surgical intervention, except where obstruction is due solely to the enlargement of lymph glands in the course of infectious disease, or is a manifestation of metastatic

malignancy or a generalized process such as Hodgkin's disease, will invariably result in irreparable liver damage and may prove fatal. Brief mention should be made of obstructive jaundice secondary to congenital atresia of the bile duct or ampulla. Although uncommon, this condition should be immediately diagnosed in infants presenting feeding difficulties almost immediately after birth, difficulties associated with the gradual but steady appearance of icterus. The only condition to be considered in differential diagnosis is that of icterus neonatorum which can be readily diagnosed by appropriate blood studies and the demonstration of an acholuric jaundice. Immediate surgical intervention is necessary to correct the condition of atresia. In any severe obstructive episode, a necessary *preparation for successful surgery is the adequate use of vitamin K and the availability of fresh whole blood for transfusion during the operative procedure.

CHRONIC DISEASE OF THE LIVER (CHRONIC HEPATITIS, CIRRHOSIS).—Chronic liver disease may be the result of previous damage by toxic agents, specific infections, progressive degenerative disease, prolonged partial obstruction to the flow of bile, and various types of vascular disturbances. The disease process may continue for months following an acute episode of liver damage, in which case it is usually classified as chronic hepatitis. Repeated insults or a continuation of the original process may result in a slowly progressive alteration in the entire structure of the liver, with the constant balancing of destructive and reparative processes and resulting fibrosis. This may be properly considered a chronic hepatitis as has been suggested by Bloomfield, although it is more commonly classified under the heading of cirrhosis. Inasmuch as the term *cirrhosis* implies only a chronic fibrosing change in the liver, the term has lost its original significance of a disease entity. It should serve merely as a descriptive term for late and far advanced hepatic disorders, characterized by profound structural changes in the organ and ultimately, marked deforming sclerosis. Whatever the underlying cause, chronic hepatitis or cirrhosis represents the composite result of destruction and repair. The actual replacement of degenerated or destroyed parenchymal tissue may be adequate in amount, in which event hepatic function may be competent and the condition may be described as compensated. Replacement of liver damage by scar tissue and, in fact, excessive regeneration of parenchymal cells may interfere with the intrinsic blood supply of the various functioning units of the liver and eventually result in greater or lesser degrees of hepatic incompetence. Furthermore, scar-tissue *formation may* compress the portal radicles in the liver, with resulting portal hypertension and the formation of varicosities, particularly in the esophagus *and the upper gastrointestinal tract but also* in the inferior hemorrhoidal veins. The varicosities provide a source of future danger from hemorrhage. In the final analysis the duration of survival in the presence of chronic liver disease will depend upon the existence of a sufficient number of functioning units, old or new. It is essentially a quantitative problem. If the repair process is quantitatively adequate, compensation results provided the demands of the individual patient do not exceed the ability of the liver to meet metabolic requirements. If regeneration has not been quantitatively adequate, then symptoms of hepatic insufficiency appear with measurable loss of specific liver function.

In general, the outstanding symptom of chronic liver disease is that of easy fatigability due to a failure to meet general metabolic requirements. In addition, specific symptoms and signs appear in decompensated cirrhosis as the result of very special hepatic activities. Thus a normocytic anemia with a lowering of the red-cell count and the hemoglobin, is commonly encountered. At times the anemia may be macrocytic due to lack of ability to provide the factor necessary to mature erythrocytes. Hypoprothrombinemia may be present with resulting spontaneous hemorrhages and purpura, and failure to conjugate estrogens may result in gynecomastia, testicular atrophy and loss of axillary hair. Jaundice may be present due solely to a widespread interruption of normal canalicular continuity. Vascular *changes may occur resulting* in the formation of spider angiomata and the appearance of so-called liver palms. Peripheral edema

ascites and hydrothorax may appear because of a reduction in plasma osmotic pressure secondary to a lowering of serum albumin An added factor in the production of ascites is undoubtedly the existence of portal hypertension Neither the factor of a lowered plasma osmotic pressure nor that of portal hypertension alone can be held responsible for this phenomenon Regardless of the type of disease underlying the chronic hepatic disturbance episodes of fever are not uncommon They can be most reasonably explained on the hypothesis that the liver is unable by its normal bacteriolytic processes satisfactorily to handle organisms coming to it from the digestive tract Episodes of pain that are entirely comparable to attacks of biliary colic are occasionally encountered These may at times be due to a sudden stretching of the liver capsule but more frequently than not no satisfactory explanation can be adduced other than the fact that chronic liver disease exists Weakness on exertion may be extreme and at times episodes simulating attacks of hypoglycemia occur episodes which may even result in temporary unconsciousness Itching may be present in any form of chronic liver disease either with or without jaundice although as a rule it is associated with evidences of external obstruction to the flow of bile

The physical signs of chronic liver disease are essentially those which have already been discussed They will vary tremendously according to the stage of the disease that exists at the time of examination Alterations discovered through laboratory tests undergo similar variations Generally in compensated liver disease the most common findings are moderate anemia slight bromsulphalein retention positive results in the flocculation tests and a tendency to a lowering of the serum albumin Hyperbilirubinemia is not a feature unless chronic partial obstruction exists When the intrahepatic process undergoes an exacerbation of its activity all functional tests become more abnormal and if there is active degeneration of parenchymal tissue hyperbilirubinemia increases usually in association with tenderness and enlargement of the liver Intercurrent infection hemorrhage operative procedures and the use of drugs that may be toxic to the liver commonly result in exacerbations of the underlying disease with an increase in symptoms and marked alterations of all functional tests For example an attack of pneumonia in a patient with compensated cirrhosis or an unavoidable surgical operation may be immediately followed by the appearance of jaundice liver enlargement ascites and peripheral edema Major hemorrhage from esophageal varices or from any other source may be associated with similar abrupt changes and the tendency to ascites and edema may be intensified by the loss of plasma albumin and the replacement of fluid by physiological saline It is to be noted that following severe hemorrhage in patients with cirrhosis and splenic enlargement there may be a temporary but striking reduction in the size of the spleen One point of extreme importance is that the appearance of edema, and particularly of ascites, is not necessarily an irreversible phenomenon Ascites may appear merely as an acute transient phenomenon that is entirely reversible It may not recur for months or years and then only as a result of further serious liver damage In the presence of chronic liver disease the disappearance of ascites under proper medical management provides in itself a very hopeful prognostic fact

Chronic hepatitis or cirrhosis may be classified for practical purposes under six headings (1) post atrophic cirrhosis (2) Laennec's or portal cirrhosis (3) biliary cirrhosis (4) syphilitic cirrhosis (5) cardiac cirrhosis and (6) parasitic cirrhosis

### Post-atrophic Cirrhosis

Post atrophic cirrhosis as the name implies is the late result of progressive continuing chronic hepatitis presumably viral in origin Undoubtedly cases also occur as the result of the action of specific poisons in initiating degenerative changes From the case history one may be able to obtain a continuous story of liver disease covering months or years starting with a typical attack of infectious hepatitis In many instances such a history is lacking and the

malignancy or a generalized process, such as Hodgkin's disease, will invariably result in irreparable liver damage and may prove fatal. Brief mention should be made of obstructive jaundice secondary to congenital atresia of the bile duct of ampulla. *Although* uncommon, this condition should be immediately diagnosed in infants presenting feeding difficulties almost immediately after birth, difficulties associated with the gradual but steady appearance of icterus. The only condition to be considered in differential diagnosis is that of icterus neonatorum, which can be readily diagnosed by appropriate blood studies and the demonstration of an acholuric jaundice. Immediate surgical intervention is necessary to correct the condition of atresia. In any severe obstructive episode, a necessary preparation for successful surgery is the adequate use of vitamin K and the availability of fresh whole blood for transfusion during the operative procedure.

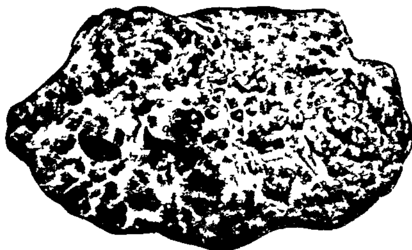
CHRONIC DISEASE OF THE LIVER (CHRONIC HEPATITIS, CIRRHOSIS).—Chronic liver disease may be the result of previous damage by toxic agents, specific infections, progressive, degenerative disease, prolonged partial obstruction to the flow of bile, and various *types of vascular disturbances*. *The disease* process may continue for months following an acute episode of liver damage, in which case it is usually classified as chronic hepatitis. Repeated insults or a continuation of the original process may result in a slowly progressive alteration in the entire structure of the liver, with the constant balancing of destructive and reparative processes and resulting fibrosis. This may be properly considered a chronic hepatitis, as has been suggested by Bloomfield, although it is more commonly classified under the heading of cirrhosis. Inasmuch as the term *cirrhosis* implies only a chronic, fibrosing change in the liver, the term has lost its original significance of a disease entity. It should serve merely as a descriptive term for late and far-advanced hepatic disorders characterized by profound structural changes in the organ and, ultimately, marked deforming sclerosis. Whatever the underlying cause, chronic hepatitis or cirrhosis represents the composite result of destruction and repair. The actual replacement of degenerated or destroyed parenchymal tissue may be adequate in amount, in which event hepatic function may be competent and the condition may be described as compensated. Replacement of liver damage by scar tissue and, in fact, *excessive regeneration of parenchymal cells* may interfere with the intrinsic blood supply of the various functioning units of the liver and eventually result in greater or lesser degrees of hepatic incompetence. Furthermore, scar tissue formation may compress the portal radicles in the liver, with resulting portal hypertension and the formation of varicosities, particularly in the esophagus and the upper gastrointestinal tract but also in the inferior hemorrhoidal veins. The varicosities provide a source of future danger from hemorrhage. In the final analysis, the duration of survival in the presence of chronic liver disease will depend upon the existence of a sufficient number of functioning units, old or new. It is essentially a quantitative problem. If the repair process is quantitatively adequate, compensation results, provided the demands of the individual patient do not exceed the ability of the liver to meet metabolic requirements. If regeneration has not been quantitatively *adequate, then symptoms of hepatic insufficiency* appear, with measurable loss of specific liver function.

In general, the outstanding symptom of chronic liver disease is that of easy fatigability due to a failure to meet general metabolic requirements. In addition, specific symptoms and signs appear in "decompensated cirrhosis" as the result of very *special hepatic activities*. Thus, a normocytic anemia with a lowering of the red-cell count and the hemoglobin is commonly encountered. At times, the anemia may be macrocytic due to lack of ability to provide the factor necessary to mature erythrocytes. Hypoprothrombinemia may be present, with resulting spontaneous hemorrhages and *purpura*, and failure to conjugate estrogens may result in gynecomastia, testicular atrophy, and loss of axillary hair. Jaundice may be present due solely to a widespread interruption of normal canalicular continuity. Vascular changes may occur, resulting in the formation of spider angiomata and the appearance of so-called *liver palms*. *Peripheral edema*

PLATE IX



A



B

Portal Cirrhosi Nodular Hyperplasia

A ~urface iew B Cut ection green area re n rated nod iles with b le retention

*L chtman D as s of the L r)*

presumption is that the original insult occurred during an acute attack of an unrecognized, non icteric infectious hepatitis. The history may reveal exposure to known toxic substances, such as carbon tetrachloride, chloroform, cincophen, and the like. Typically, there is moderate enlargement of the liver and spleen, but, as the disease continues, the liver becomes progressively smaller until it can be demonstrated only with difficulty on physical examination. Unless the diagnosis is suggested by history or by histological study of tissue obtained by aspiration biopsy, the condition is clinically indistinguishable from Laennec's cirrhosis. Grossly and microscopically, the liver architecture is tremendously altered with evidence of widespread liver necrosis and regeneration. Irregular lobules of regenerated liver cells will be noted with condensation of bile ducts and liver reticulum and with large bands of connective tissue. The entire picture is that of a disorderly arrangement of liver structure which can usually be recognized by an experienced pathologist as the result of a preceding acute atrophic process.

The course of the disease is usually marked by remissions and exacerbations with gradually increasing failure of function. Varying degrees of jaundice are usually present and an elevated temperature commonly accompanies exacerbations. Ascites is a relatively late manifestation. Various therapeutic measures are ordinarily less effective in restoring liver competence than they are in cases of the more common alcoholic cirrhosis. Therapy consists more or less in limitation of activity, depending upon the stage of the disease, the provision of an adequate diet and specific replacements. The condition tends to be one of relentless progression with eventual and complete liver failure. Esophageal varices may occur late in the disease, and gross hemorrhage from this source may necessitate consideration of surgical intervention.

One therapeutic measure should be watched with interest. In a few instances ACTH has been employed in the earlier stages of the disease with apparent interruption of the process and an improvement in symptoms and hepatic functions. ACTH must be used only with great caution inasmuch as the tendency of this preparation to cause increased proteolysis and sodium retention may readily produce unfavorable complications. With very adequate supervision, however, it is conceivable that the cellular changes accompanying the morbid conditions terminating in post atrophic cirrhosis may be halted or modified to an important degree by the careful use of this or similar substances.

### Laennec's Cirrhosis (Portal Cirrhosis, Alcoholic Cirrhosis)

This condition is by far the most common form of chronic liver disease throughout the world. The causative factors are undoubtedly multiple, but it is highly probable that the initial changes in the liver may be assigned to nutritional deficiency as a primary etiological factor. That such can be the case is evident from the careful studies of Gillman and Gillman and many others on infants and children developing full blown and often fatal cirrhosis in association with striking dietary lack. The complete reversibility of the process in early cases by the use of well balanced diets alone, further strengthens such a conception. Instances of chronic degenerative liver disease apparently caused by dietary deficiency have gradually been multiplied in various parts of the world and bear close resemblance to the results obtained by animal experimentation in which specific deficiencies in such substances as methionine, choline, and total protein have produced analogous changes. In adult human beings, additional factors undoubtedly play an important role. It is still highly controversial whether alcohol as such is a causative factor in the production of portal cirrhosis. It is undoubtedly true that a large percentage of adult cases of Laennec's cirrhosis have never used alcohol in any form. Nevertheless alcohol may act as a causative factor and when used to excess usually is accompanied by an inadequate intake of protein and total calories. Certainly intercurrent infections may play an additional role in the presence of prolonged undernutrition. Chronic diarrhea due to such conditions as chronic ulcerative

colitis or chronic dysentery may provide the background for malnutrition and hyperthyroidism of long duration and severe grade may increase metabolic activity to such an extent that the dietary intake may be quite inadequate In any event it is safe to say that the most common single factor that can be observed in patients with portal cirrhosis is that of an inadequate diet with a particular deficiency in protein and lipotropic substances The important implication of and relatively few lobules of normal parenchymal tissue The early stages may be open to controversy The so-called fatty liver may represent the initial phase of this type of liver disease although this is not at all sure In the fatty liver the liver lobules characteristically contain large numbers of polygonal cells filled with fat droplets of varying size Little or no degenerative change may be found It is possible that a continuation or frequent repetition of this



FIG 210 —Fatty infiltration Cellular degeneration Connective tissue proliferation Recovery from the effects of alcohol (biopsy of human liver) (Connor courtesy of Am J Path )

these considerations is that the disease process should be a relatively reversible one in the early stages if an adequate diet is provided

The pathological changes characteristic of Laennec's cirrhosis are those of a gradually progressive degenerative disease with more orderly processes of repair than those usually encountered in post atrophic cirrhosis The late stages may be essentially identical with the production of a hobnailed liver and histological changes *showing striking fibrosis* process may result in necrosis of individual cells in increasing numbers with repair and eventually accompanying fibrosis and scar-tissue formation During the course of portal cirrhosis the processes of hepatic-cell degeneration fatty infiltration and at times the tremendous outpouring of leukocytes into areas of necrosis are constantly recurring events Connective-tissue proliferation may involve the capsule of the liver the portal areas and the central areas of the lobules including the central veins

fat from the polygonal cells with the clearing up of an active degenerative process and with associated adequate repair of damage Obviously complete reversal of the degenerative process can be obtained only in very early cases It should be emphasized that not infrequently very early manifestations of hepatic degeneration may be extremely acute with fever jaundice right upper-quadrant pain and even ascites Under these conditions profound changes in the liver parenchyma are present which may be almost completely restored to normal by appropriate intensive therapy In the acute manifestations of the disease the use of intravenous injections of hypertonic glucose may be very effective for a few days until the patient can take an adequate diet by mouth The anemia that is a rather constant accompaniment of the later stages of the disease responds very poorly to massive doses of either iron or liver Transfusions are frequently of help as a symptomatic measure and are absolutely essential when active bleeding from varicosities has occurred When ascites is encountered and is of recent origin dietary measures plus the use of a low sodium intake are frequently effective In most resistant cases help may be obtained by the use of mercurial diuretics with or without the preceding use of ammonium chloride or similar preparations Where ascites tends to recur as a result of exacerbations of the underlying process or because of intercurrent infection it may prove to be relatively intractable but may respond temporarily if a low serum albumin is raised by the intravenous infusion of human salt free serum albumin This is an extremely expensive maneuver and in itself offers only transient help When ascites is present it is wise not to remove the accumulated abdominal fluid by paracentesis unless the volume of fluid is so great as to interfere with eating or is the cause of intolerable abdominal discomfort It is much wiser as a rule to attempt all possible medical measures before resorting to paracentesis In the later irreversible stages of the disease at times the only effective measure is that of repeated abdominal taps but under such circumstances it is obvious that the disease is far advanced in its course As an aid to the maintenance of low sodium levels the use of, ion-exchange resins may be of help It should be remembered however that they can be employed only under careful supervision and with the knowledge that they may result in a sharp reduction in sodium or potassium to a point where symptoms arise from this fact alone The recent introduction of cation-exchange resins fortified with potassium may make it possible to obviate the danger of producing sudden hypopotassemia

As already noted the development of portal hypertension results in the eventual production of engorged venous channels particularly in the form of esophageal varices and internal hemorrhoidal veins Massive bleeding may occur from either of these sources but dangerous bleeding is rarely encountered from the latter In recent years the performance of anastomotic shunts between the splenic or portal veins and the systemic circulation has given promise of an important source of protection against exsanguinating hemorrhage from these sources The work of Blakemore and of Linton during recent years has produced convincing evidence that splenorenal and portocaval shunts are of immense value when performed in carefully selected cases by extremely competent surgeons The danger of such surgery is obvious and the contraindications are clear Patients with active disease as evidenced by the presence of jaundice fever or intractable ascites probably are poor subjects for such a procedure When serum albumin values are below a level of 3 0 grams per cent the risk is very great and operation should be avoided unless there is improvement under routine intensive medical therapy If the development of ascites is of recent occurrence and follows a major hemorrhage medical measures may restore the liver to good compensation the albumin level may rise and at that point operation may properly be performed The operation should not be attempted except by adequately trained surgeons An important safeguard to the success of the operation is the employment of absolutely fresh whole blood during the operative procedure

The occurrence of acute exsanguinating

In compensated cases fatty infiltration of the parenchymal cells is frequently lacking In the late stages of the disease fibrosis predominates with a steady and marked reduction of the islands of polygonal cells, which may be subdivided into small compartments by the encroachment of connective tissue Compression of portal vein radicles is an obvious result with the development of extreme degrees of portal hypertension and enlargement of esophageal and frequently, gastric veins

Physical findings will depend entirely on the stage of the disease In the earlier stages, the liver is large and firm The edge of the liver is rounded, and the spleen typically shows only moderate increase in size Except in what might be called an active stage of the degenerative process, jaundice is lacking and hepatic tenderness is absent As reparative processes are less effective and fibrosis increases the liver typically becomes smaller and harder the spleen continues to enlarge and portal hypertension becomes evident by the appearance of a collateral circulation which can be visualized in the abdominal wall and over the lower thorax Ascites may appear but, under proper management may be only a temporary phenomenon It may be preceded by the appearance of peripheral edema which at times is incorrectly treated as evidence of cardiac or renal failure Spider angiomata appear in groups over the face, thorax, and upper extremities Bleeding may occur from the gums or the nose, from dilated veins in either the esophagus or the stomach or from internal hemorrhoids Intermittent short episodes of fever and abdominal pain may be encountered from time to time

The diagnosis will be made on the basis of a history of chronic alcoholism or dietary deficiency, or both plus the evidence of hepatic damage as manifested by the various symptoms and signs that have already been discussed In advanced cases even in the absence of bleeding it is always of importance to give the patient a swallow of barium in order to determine the presence or absence of esophageal varices Deviations from normal in all the tests of hepato cellular function may be encountered and the degree of abnormality will depend entirely upon the stage of the disease In cases of fatty liver and in the very early stages of portal cirrhosis there may be little or no abnormality in the results of tests of hepatic function, except possibly in the retention of bromsulphalein Subsequently, more and more laboratory evidence of hepatic insufficiency can be obtained The presence of jaundice hypoprothrombinemia which does not respond to the administration of vitamin K and a slow, progressive drop in serum albumin are always bad prognostic signs The finding of esophageal varices obviously suggests the possibility that fatal hemorrhage may occur at any time, regardless of the state of the liver

*Treatment* —The therapeutic principles already discussed are particularly effective in the treatment of this type of liver disease Convincing evidence of this may be found in the occasional patients in whom abdominal surgery reveals a hitherto unsuspected and totally compensated hepatic cirrhosis Such a finding clearly indicates that the disease may go on for years without causing any symptoms and without receiving any particular treatment When the disease is diagnosed because of early symptoms or signs, the most important therapeutic measures are the avoidance of overfatigue and the administration of a diet adequate in calories and high in protein If the diet is well balanced all necessary vitamins will be automatically included with the possible exception of vitamin K Furthermore the ingestion of a diet high in protein insures an adequate supply of lipotropic substances such as methionine and choline Avoidance of overactivity with resulting fatigue and the provision of an adequate diet, therefore constitute the cornerstone of therapy To this must be added the necessity of avoiding specific hepatotoxins The use of alcohol should be regarded with suspicion and probably should be completely prohibited Even in cases in which jaundice and ascites are present intensive and continuous therapy will frequently result in disappearance of these conditions restoration of liver function and the production of a compensated cirrhosis Serial liver biopsies have demonstrated conclusively that these measures are effective in promoting the disappearance of

be distinctly abnormal and disturbances of hepatocellular function may be completely absent. Later parenchymal-cell damage will obviously be associated with abnormalities of hepatocellular function.

*Treatment* is primarily surgical and whenever possible, attempts should be made to provide adequate drainage of the external biliary ducts either by removal of the obstruction or by plastic measures providing a new communication of the dilated common duct to the duodenum or jejunum. In this particular group of patients there is little doubt that the careful use of antibiotics, particularly chloromycetin and possibly aureomycin, may be effective in controlling episodes of cholangitis with chills, fever and pain. Under such treatment fever may disappear and the enlarged and tender liver may become somewhat reduced in size and completely or relatively insensitive to palpation. Antibiotic therapy is a proper protective measure preliminary to operation. In the rare event that the disease progresses to the point of massive hemorrhage from esophageal varices, shunt surgery can be considered and has on occasion been successfully performed.

CHOLANGIOLITIC BILIARY CIRRHOSIS.— This extremely rare condition differs from obstructive biliary cirrhosis in that the evidences of obstruction are entirely confined to the internal structure of the liver. It occurs in younger adults. The etiology is not known.

*Morbid Anatomy*.—Pathological changes are initially limited to the bile canaliculi which show evidences of cholangitis or pericholangitis with bile stasis. As the disease progresses degenerative changes may occur in the parenchyma with consequent repair and fibrosis. Enlargement of the liver and spleen is pronounced. The external bile ducts are essentially normal.

*Symptoms and Signs*.—The initial symptoms are variable. They may be similar to those of infectious hepatitis or they may be characterized by a series of attacks of fever, jaundice and right upper-quadrant pain with enlargement of the liver and spleen. Occasionally the only presenting symptom is intense itching which may persist for many months before the occurrence of jaundice is noted. Once the disease is well established pruritis is a rather constant and very distressing symptom. The late stages of the disease may be accompanied by evidences of hepatic insufficiency and by the development of portal hypertension. An interesting but rare complication of this condition as well as that of obstructive biliary cirrhosis is the gradual decalcification of the bony structure with spontaneous fractures. In spite of the typical and persistent appearance of jaundice the stools usually contain moderate amounts of bile pigment and may be of almost normal color. Except in the late stages of the disease laboratory examinations reveal evidences of disturbed excretion of bile products. Alkaline phosphatase and serum cholesterol may reach very high levels. As in other chronic forms of liver disease clubbing of the fingers is occasionally seen. The jaundice tends to be a dark brown or greenish jaundice and the skin frequently becomes extremely dark due to deposition of melanin. Xanthomata are frequently present around the eyes and in the flexures of the skin of the hands, elbows and knees; they may be very painful.

The disease progresses slowly but is usually fatal within a period of from eight to ten years. Except for supportive measures therapy is largely symptomatic. When itching is extreme experience has shown that prolonged T tube drainage of the common duct may result in considerable relief of this symptom. An interesting fact is that such drainage may also be accompanied by the complete disappearance of the xanthomata.

The term *Hanot's cirrhosis* has been loosely applied to this condition and occasionally to that of obstructive biliary cirrhosis. Any exact definition of Hanot's cirrhosis based on his original article is absolutely impossible and the term should be avoided.

SYPHILITIC CIRRHOSIS (HEPAR LOBATUM)

True syphilitic cirrhosis is a manifestation of late acquired syphilis and is the result of gummatous involvement with fibrosis and the production of coarse lobulation of the organ. With earlier diagnosis and improved methods of treatment this manifestation of

bleeding from esophageal varices in itself constitutes a serious acute emergency If bleeding does not stop spontaneously within a reasonable period of time, compression of the coronary veins by tamponade with an inflated balloon may be a life saving procedure The actual ligation of bleeding varices has been successfully performed in a few instances by the transthoracic surgical approach When hematemesis from esophageal varices occurs oral feeding should be avoided for several days in contradistinction to the use of small frequent feedings that may properly be employed in instances of hemorrhage from diffuse gastritis or peptic ulcer Obviously blood lost by bleeding from varices must be replaced

One final consideration is the treatment of intermittent episodes of fever having no other determinable cause than the presence of cirrhosis In a few cases the use of chloromycetin over a period of several days has adequately controlled febrile episodes and has definitely improved the condition of the patient

*Course* —As already implied the course of the disease is variable but it may progress over a period of very many years With a newer understanding of the principles of treatment of hepatic disease it is important to adopt an optimistic attitude and employ intensive dietary and replacement measures until any evidence of a response is lacking It will frequently be a matter of surprise to the physician that such measures will restore an obvious cirrhotic to many months or years of useful living

## Biliary Cirrhosis

Obstructive Biliary Cirrhosis —Obstructive biliary cirrhosis is a condition which develops as a result of chronic partial obstruction and infection of the large bile ducts It is relatively uncommon It is usually encountered as a result of surgical trauma to the common bile duct or in patients with common duct stone of long standing It may result from a slowly progressing constriction of the duct by surrounding adhesions, enlarged lymph glands or carcinoma, occasionally, it is the result of parasitic infestation It has been produced experimentally in animals by ligation of the common duct Whether it is due to mechanical obstruction alone, with associated back pressure in the ductal system or is caused by ductal infection which is almost invariably present, is not clear, both factors are probably operative

*Morbid Anatomy* —Unlike post atrophic cirrhosis and portal cirrhosis the liver in biliary cirrhosis is characterized by a relatively smooth surface which, on close inspection, is found to be finely granular and deeply pigmented with biliverdin The chief histological characteristics are those of striking increase in connective tissue involving the capsule and the portal areas, with interlobular extension, and by dilatation and proliferation of the bile ducts Bile stasis is usually recognized by the appearance of masses of inspissated bile in the dilated canaliculi In the advanced stages of the disease changes in the parenchymal cells occur and eventually the processes of polygonal-cell degeneration repair and fibrosis become apparent

*Symptoms and Signs* —The disease is most commonly encountered in the later decades of life, and there is usually a definite story of intermittent obstruction of many years duration with episodes of fever chills jaundice and right upper-quadrant pain Frequently initial symptoms closely follow operation on the gallbladder or common bile duct As the disease progresses anorexia nausea and vomiting may be present, and easy fatigability is common Fat loss may occur and spontaneous bleeding due to hypoprothrombinemia is encountered In advanced cases all the evidences of liver insufficiency are present and ascites and peripheral edema are to be expected Hemorrhage from esophageal varices occurs if the patient survives the disease for a period of time sufficient to produce fibrosis and portal hypertension Hepatic enlargement is relatively marked and an increase in the size of the spleen can practically always be demonstrated on careful examination Jaundice is nearly always present Laboratory findings as might be expected vary with the stage of the disease In the earlier stages those tests indicating interference with the excretion of bile and other substances will

along with other signs of cardiac insufficiency Pathologically the liver is enlarged and the capsule tense On section a reddish-gray mottling with a typical nutmeg appearance is seen Central necrosis and hemorrhage are present in severe cases Liver functions, as measured by laboratory tests are abnormal in direct relation to the degree of cardiac failure In most instances the process is entirely reversible if cardiac insufficiency can be corrected

*Acute thrombosis of the portal vein* is fortunately very uncommon It may occur in association with cirrhosis of the liver as a rare complication It may be associated with malignant disease which causes thrombosis by compression of the vein It may be secondary to an adjacent inflammatory process or may result from a specific infection such as typhoid It occurs as a fulminating incident leading to severe abdominal pain splenic enlargement ascites and hemorrhage from the upper gastrointestinal tract Fever and a striking leukocytosis are usually encountered Death may occur in a few days due to extension of the thrombotic process to the mesenteric veins

Diagnosis of the acute form of the disease is extremely difficult especially when there is a coexisting cirrhosis of the liver In the absence of a known cirrhotic process the sudden appearance of the symptoms described above together with the rapid development of signs of portal vein obstruction may give a clue to the primary underlying process

Treatment of the acute condition is usually ineffective but measures to control shock and proper use of antibiotics would seem to be indicated

*Chronic thrombosis of the portal vein* may occur without any diagnostic symptoms or signs until portal or splenic vein hypertension has developed One may be able to elicit a history of recurrent episodes of vague abdominal pain and fever following acute infections such as typhoid malaria pneumonia and the like Occasionally there may be a history of an omphalitis in infancy The process is essentially an infective thrombophlebitis of the portal vein or its radicles with resulting cavernomatous changes and at times chronic fibrosis and occlusion Evidences of a collateral circulation gradually appear with enlargement of the spleen and anemia Hemorrhage from dilated esophageal or gastric veins may be the first indication of the condition The entire symptom complex may properly be classified as Banti s disease or congestive splenomegaly Hepatic changes as a rule are minor except where a progressive cirrhotic process is associated with an active thrombophlebitis of the portal venous system Where cirrhosis is not the primary disease changes in the liver consist essentially of minor degrees of degeneration of hepatic lobules with fibrosis and diminution in the size of the organ No serious alterations in hepatic function occur If there is bleeding from esophageal varices serious consideration should be given to the possibility of adequate venous shunt surgery with a resulting reduction in portal venous pressure

*Thrombosis of the Hepatic Veins* (Budd-Chiari Syndrome) —Thrombosis of the hepatic veins is a rare condition which occurs as a result of inflammatory neoplastic or fibrotic changes in the liver or in the course of such diseases as thrombophlebitis migrans and polycythemia vera As in thrombosis of the portal vein, acute and chronic forms of the condition may be encountered Obstruction of the hepatic veins may be partial or complete Hepatic changes depend upon the completeness of the occluding process There may be marked engorgement of the liver with dilatation of the sinusoids Hemorrhages in the region of the central veins may be prominent with necrosis of the lobular tissue Acute thrombosis of the hepatic veins is accompanied by the sudden appearance of epigastric pain rapid enlargement of the liver ascites and collateral venous engorgement Fever and leukocytosis are present Because of the rapid enlargement of the liver right upper-quadrant abdominal tenderness is usually present Enlargement of the collateral veins may be extensive Jaundice is not a striking feature As a rule the condition progresses steadily with increasing impairment of hepatic function and death within a few weeks

Chronic partial thrombosis of the hepatic veins undoubtedly occurs but diagnosis of

syphilis is becoming progressively less common and, at present, is only occasionally encountered. The exact identity of hepar lobatum is controversial, and it is frequently the case that gummatous involvement of the liver, with subsequent healing, may occur in association with portal cirrhosis. In cases *in which a very grossly lobulated liver is* encountered in patients with positive serological evidence of syphilis, the diagnosis of hepar lobatum may be justified, although one is never certain that the obvious liver involvement is due solely to spirochetal disease. In the absence of evidence of diffuse liver disease with failure, such treatment should be carried out as is commonly employed in the presence of gummatous lesions. When evidences of *liver insufficiency* are present, careful supportive measures and proper replacement therapy should also be employed.

### Cardiac Cirrhosis

This condition is characterized by fibrotic changes in the liver, changes primarily localized around the central hepatic veins. It is always associated *with long standing congestive* heart failure. This may be secondary to tricuspid insufficiency, marked mitral involvement, or chronic constrictive pericarditis. Other forms of heart disease may occasionally provide the basis for the appearance of pronounced structural hepatic changes.

*Morbid Anatomy.*—On gross examination, the liver may be found to be normal in size or slightly *enlarged*. It is firm, finely nodular, and darkly mottled in color. Extensive fibrosis is evident on cut section, and histological examination shows the central areas of the lobule to be most involved, although connective tissue increase may be apparent in the portal areas as well.

*Diagnosis.*—The diagnosis is never justified unless evidences of long standing congestive failure are clear. Signs of cardiac failure are obvious, cyanosis usually being present. When associated with constrictive pericarditis, liver enlargement is usually more marked than when due to other causes of cardiac failure. Splenic enlargement is nearly always present, and engorgement of the neck veins can always be demonstrated. Ascites may be present. Laboratory tests reveal abnormalities in hepatocellular function. Jaundice is rarely present.

*Treatment* of the hepatic disease consists almost exclusively in measures directed toward improvement of the cardiac condition. Restriction of sodium in the diet is an important measure. In constrictive pericarditis, surgical decortication of the heart may *be associated with surprising improvement* in hepatic function, but it is obvious that no therapeutic measure can produce complete regression of the fibrotic process in the liver.

### Parasitic Cirrhosis

Parasitic cirrhosis of the liver is an important complication of infestation by various liver flukes, such as those encountered in *distosomiasis and schistosomiasis*. These diseases are adequately discussed in another section. In the chronic, advanced forms of liver disease secondary to liver flukes, the general principles underlying the evaluation and treatment of chronic hepatic disorders obtain.

Hemochromatosis.—Hepatic changes in hemochromatosis have been described under *Diseases of Metabolism*. It is pertinent to point out that enlargement of the liver may be the only clinical manifestation of this unusual disturbance in iron metabolism. Laboratory evidence of impairment of liver function may be obtained, but in no way indicates the cause of the hepatomegaly. Aspiration biopsy of the liver will invariably *provide the basis for a histological diagnosis* of the disease.

## DISTURBANCES OF HEPATIC CIRCULATION

Congestive Heart Failure.—Congestive heart failure almost invariably leads to transient and usually reversible hepatic changes. If the congestive failure is of extreme degree and of long standing, it may result in a true fibrotic process which *has* already been described as cardiac cirrhosis. *The usual manifestations of congestive* failure are those of slight hepatic enlargement, frequently with tenderness over the liver

along with other signs of cardiac insufficiency Pathologically the liver is enlarged and the capsule tense On section a reddish gray mottling with a typical nutmeg' appearance, is seen Central necrosis and hemorrhage are present in severe cases Liver functions as measured by laboratory tests are abnormal in direct relation to the degree of cardiac failure In most instances the process is entirely reversible if cardiac insufficiency can be corrected

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the condition is rarely possible prior to death It may be suspected in cases in which there is hepatic enlargement or extensive collateral circulation and intractable ascites, without evidence of splenic enlargement There is no satisfactory treatment of either the acute or the chronic type of the disease

HEPATOLENTICULAR DEGENERATION (WILSON'S DISEASE) —This curious combination of lenticular degeneration of the brain and portal cirrhosis is extremely rare It tends to occur in families and becomes apparent in the early decades of life Evidences of liver impairment vary considerably in individual cases and the course of the disease follows the usual pattern of portal cirrhosis There is some suggestion that disturbances in copper metabolism may be involved in the production of the condition, which has been more fully discussed under *Organic Diseases of the Nervous System* When symptoms of liver impairment are present general measures already discussed may be employed As a rule, they are relatively ineffective

TUMORS OF THE LIVER —Tumors of the liver include benign cysts benign cellular tumors, primary carcinoma and metastatic carcinoma

*Benign cysts of the liver* are not productive of symptoms and are diagnosed only at operation for some other condition The origin of such cysts is not known and no therapy is indicated Hepatic cysts may occur in association with cystic disease of the kidneys Echinococcus disease is a common cause of cysts in the liver and has been discussed in the section on *Metazoan Diseases*

*Benign cellular tumors of the liver* are uncommon and comprise benign adenomata and hemangiomata Neither type of tumor produces symptoms or interference with hepatic function The diagnosis is usually made by accident at the time of abdominal exploration Bleeding following trauma may occur from hepatic hemangiomata

*Primary carcinoma of the liver* is of two types (1) liver-cell carcinoma (primary hepatoma) and (2) duct cell carcinoma (cholangioma) The liver cell carcinoma is much more common than that arising from the bile ducts Primary hepatoma may occur in the absence of other disease of the liver but it is usually associated with portal cirrhosis or with the types of cirrhosis that are manifestations of infestation by liver flukes

It is relatively common in certain Asiatic countries and in other sections of the world where schistomiasis and distomiasis are prevalent In the United States, it is nearly always associated with portal cirrhosis of long standing It usually occurs in men over the age of fifty Duct-cell carcinoma is more frequently seen in women and may appear as a late manifestation of long standing cholangitis or biliary cirrhosis

Symptoms of primary carcinoma of the liver do not differ significantly from those of the underlying cirrhosis The existence of a malignant tumor may be suspected by the steady increase in size of particular areas of the liver which may occasionally become frankly nodular Jaundice may or may not be a striking feature but it usually is present and is apt to increase steadily in intensity Anorexia weakness and loss of weight occur at a rate more rapid than that expected in the natural course of the underlying cirrhotic process Abdominal or back pain may be a feature and palpation of the liver frequently demonstrates tender areas Ascites may be manifest and the ascitic fluid is frequently hemorrhagic and of high specific gravity it may also contain tumor cells Upper abdominal films may show lobulation of the liver outline Liver function tests are in no way diagnostic but aspiration biopsy of the liver may frequently provide proof of malignant disease Medical treatment is entirely palliative and attempts to resect involved areas are of dubious value

*Secondary carcinoma of the liver* is common Metastases may be derived from primary neoplasms of the esophagus, stomach pancreas colon and biliary passages Occasionally hepatic metastases are secondary to cancer of the breast Metastatic nodules may be few in number or may involve a very large proportion of the organ with compression of hepatic units and resulting necrosis intrahepatic hemorrhage and jaundice The liver may be extremely large Individual nodules may be easily felt and may be tender to palpation Splenic enlargement is extremely uncommon Ascites is frequent and the fluid like that associated with primary malignancy of the liver is usually of

high specific gravity It contains easily demonstrable red cells and occasionally malignant cells Involvement of the liver may on rare occasions be so extreme as to produce portal hypertension and esophageal varices with bleeding

The symptoms associated with metastatic malignancy of the liver are those of the primary disease plus those associated with focal or diffuse liver involvement Liver function tests may yield entirely normal results or results notably deranged due to very extensive involvement of the organ Hitherto unsuspected neoplasia may be *diagnosed from histological study of the* material obtained by *punch biopsy* of the liver Therapy is almost entirely palliative in nature On rare occasions when abdominal exploration has revealed solitary implants of metastatic disease in the liver radical resection may be justified and may retard the course of the disease

Abscess of the Liver —Abscess of the liver may be due to parasitic infestation by Entameba histolytica or may be secondary to extra hepatic pyogenic infection The hepatic manifestations of amebiasis have been discussed *in the section on Protozoan Disease* Pyogenic abscess of the liver is usually associated with suppurative processes secondary to appendicitis cholelithiasis and cholecystitis It may occur as a result of systemic infection or by direct association with a penetrating wound Occasionally amebic abscesses become infected with pyogenic organisms The causative factor is usually E coli or a Gram positive coccus Infection may reach the liver by way of the portal vein it may ascend by way of the hepatic ducts or may be brought to the *liver through the hepatic artery* Liver abscesses are usually multiple

*Symptoms* —Pyogenic infection of the liver with abscess formation is characterized by a septic type of temperature accompanied by shaking chills profuse sweating and extreme weakness Nausea and vomiting may occur In severe cases abdominal distention with adynamic ileus is present *The liver may be moderately enlarged* and is nearly always tender to palpation Indeed the most characteristic sign is that of pain produced by bimanual compression of the lower right thorax Jaundice may occur but may be completely absent Ascites may be noted in severe cases especially in those associated with pylephlebitis The facial expression of the patient is drawn and gives evidence of fatigue and prostration Marked leukocytosis is to be expected

*Diagnosis* is always to be suspected in the presence of a septic temperature hepatic enlargement and tenderness and a recent story of appendicitis or cholecystitis The condition often follows operation for the above diseases Although the diagnosis is usually made on clinical grounds confirma*tion of the condition may be obtained in rare* instances by *radiological studies* of the liver after the intravenous injection of thorotrast Such an examination may reveal discrete punched out areas in the liver

*Treatment* —The outlook is always extremely grave but intensive chemotherapy and the use of antibiotics has undoubtedly modified the course of the condition Surgical drainage of single or multiple large abscesses may be possible but the intensive use of sulfadiazine penicillin and streptomycin is an indispensable therapeutic measure

## DISEASES OF THE GALLBLADDER AND BILE DUCTS

Pathological conditions involving the gallbladder and bile ducts are primarily associated with inflammatory disease Benign or malignant tumors may occur but are relatively very uncommon Infection of the gallbladder may occur in the course of other infectious disease such as typhoid fever or it may appear without known etiology In *the vast majority of instances* inflammation of the gallbladder and ducts is secondary to the presence of biliary calculi Symptoms result from the presence of local inflammation and from interference with the normal flow of bile from the gallbladder or the external hepatic ducts or common bile duct In addition to evidences of infection cholecystic and choledochal disease are usually accompanied by pain referred to the right upper abdominal quadrant or to the epigastrium with radiation to the right subscapular area or to the mid back The

appearance of jaundice is a variable finding. It may be completely absent, or it may be intense because of almost complete obstruction to the flow of bile into the duodenum. Wherever any *degree of obstruction* exists in the ductal system, infection is invariably present.

Tests of gallbladder function can be made by cholecystography following the oral administration of tetraiodophenolphthalein. This dye is absorbed into the portal circulation and excreted almost completely in the bile. When the gallbladder is normal or has not lost its powers of concentration because of chronic inflammatory disease and fibrosis, the dye will appear as a radio-opaque shadow, filling the entire organ. The administration of a *fat-containing meal will result* in prompt contraction of the gallbladder if function is normal. If the concentrating and contractile power of the gallbaldder has been lost by chronic disease or if a stone occludes the cystic duct, then dye will fail to reach the gallbaldder and no shadow will be noted. *Such a finding*, if confirmed by a second examination, will justify the diagnosis of nonfunctioning gallbladder. When stones are present in the gallbladder and concentrating function is not lost, gall stones may show as contrasting radiolucent areas, particularly if the stones are of high cholesterol content. Stones with high calcium content may be seen as very opaque shadows in the region of the gallbladder or may be actually demonstrable after cholecystography in the dye-filled organ. It is important to remember that films taken in the upright position after cholecystography may reveal a layer of translucent cholesterol stones in the fundus that were previously not demonstrable on routine horizontal films. Cholecystography provides the best means of determining gallbladder function and demonstrating biliary calculi. Another diagnostic procedure of greater difficulty and of less value is that of duodenal drainage. Material obtained during intubation of the duodenum may, on centrifugation, show microscopic evidence of cholesterol- or calcium bilirubin crystals in abundance. Such a finding in most instances gives definite indication of calculus formation. *This* method is of particular value in cases in which previous cholecystectomy has been performed and in which clinical symptoms suggest the possibility of remaining gravel or calculi in the common bile duct. In a very special group of cases duodenal drainage is of importance in determining the presence of pathogenic bacteria. In typhoid carriers, cultures *obtained by duodenal drainage are practically* always positive and diagnostic.

CHOLELITHIASIS.—Biliary calculi are commonly composed of cholesterol or calcium bilirubin, or a combination of these two elements. Rarely, gall stones may be composed solely of calcium carbonate or calcium oxylate. Stones composed entirely of bile pigment are relatively uncommon and are found only in cases of jaundice due to hemolytic disease. *With the exception of pure* pigment stones the exact etiology of gall stones is not clear. Infection may play an important role in altering the chemical and physical characteristics of bile with precipitation of crystalline material that subsequently provides the basis for calculus formation. The most obvious example of such a process is that which occurs in typhoid carriers. Almost invariably typhoid carriers who harbor the infection in the gallbladder show evidence of chronic gallbladder infection and calculus formation. Frequently viable typhoid bacilli may be found in the gall stones. Metabolic disorders such as those occurring in diabetes mellitus may provide at least a partial explanation of *calculus formation. In diabetes mellitus* disorders of lipid metabolism are common with high levels of cholesterol in the blood and bile. The very frequent occurrence of gall stones in diabetics suggests that such a relationship may be important. Similarly the factors underlying obesity may alter the concentration of *cholesterol and lipids in the* bile with resulting calculus formation. Multiple pregnancies have been considered as a possible cause of altered bile chemistry with gall-stone formation. It is probable that numerous factors influencing the concentration of one or another element of the bile *over long periods of time may be re*sponsible for calculus formation.

Biliary calculi are found in between 5 and 10 per cent of all persons coming to autopsy. They are more frequently present in women

than in men possibly due to the greater incidence of obesity and the effect of repeated pregnancies Stones may be single or multiple Large single stones are common but numerous small calculi are frequently found in the gallbladder and/or the common duct When pigment stones alone are present they occur in great numbers and are usually of very small size

*Symptoms* of cholelithiasis are usually characteristic but gall stones may be present for many years or throughout the major portion of life without producing any subjective disturbances The most characteristic symptom associated with cholelithiasis is that of biliary colic This occurs as a single episode or as frequently repeated attacks of right upper-quadrant abdominal pain However the pain may be epigastric in location or may radiate under the right scapula In rare instances biliary colic may be experienced only in the right subscapular area Occasionally the pain is experienced just below the xiphoid with radiation into the left shoulder and down the left arm completely simulating the pain of angina pectoris In very unusual cases the pain may be felt only in the left upper quadrant or in the lower abdomen The most characteristic feature of biliary colic is the fact that it usually occurs without preceding symptoms of importance gradually increases in severity then diminishes and finally disappears leaving residual tenderness in the right upper quadrant The duration of a given attack may be limited to a relatively few minutes but typically it lasts for several hours and may persist intermittently for days The pain may be relatively mild in intensity but may be so severe as to require frequent hypodermic injections of morphine for relief Nausea and vomiting are common but on numerous occasions may be secondary to the administration of morphine rather than to the underlying disease It is thought that the intake of fatty food frequently precipitates attacks of biliary colic Such a conception may be a reasonable one since the ingestion of fatty food may cause a contraction of the gallbladder It must not be forgotten however that in very many instances bladder contractility is lost because of thickening and fibrosis of the wall with obvious interference with any such pain producing mechanism Intolerance to fatty or greasy foods or to large meals and vague symptoms of "indigestion, with heartburn and belching of gas are frequently associated with cholelithiasis and are noted between attacks Whether these symptoms are secondary to biliary tract disease or to faulty dietary and bowel habits is open to question At times ulcer like symptoms are present due to reflex motor and secretory disturbances of the gastroduodenal segment In acute attacks of biliary colic fever and occasionally chills may occur but are by no means invariable

Physical signs vary extremely in individual cases The most common sign to be noted is that of focal tenderness over the region of the gallbladder Examination during an acute attack may also reveal muscle rigidity and occasionally a palpable gallbladder In the absence of jaundice the finding of a palpable gallbladder during an attack is highly suggestive of the presence of a stone temporarily impacted in the ampulla of the cystic duct with consequent obstruction to the flow of bile from the gallbladder The resulting dilatation and enlargement of the gallbladder to the point where it can be palpated may be extremely transitory this is due to the fact that the stone obstructing the cystic duct may have a ball valve action and may be shortly dislodged from its obstructing position Jaundice may occur during attacks of biliary colic as a result of one of two mechanisms It may be due to the presence of stones in the common duct causing obstruction to the flow of bile or it may be associated with cholangitis secondary to ductal obstruction or to infection spreading from the gallbladder itself In individual attacks the depth of jaundice may be relatively slight but if the attack persists with a sufficient degree of obstruction and infection jaundice may be severe and may last for days or weeks In rare instances acute abdominal pain may be due to an inflammatory process involving the peritoneum in the vicinity of the gallbladder secondary to perforation of the gallbladder or common duct As discussed under *Intestinal Obstruction* a large gall stone may penetrate the wall of the gallbladder or more rarely the

common duct and form a fistulous tract which eventually communicates with the duodenum, permitting passage of gall stones into the lumen of the intestine Intestinal obstruction from such a cause usually occurs in the vicinity of the ileocecal valve The appearance of chills in the presence of fever and biliary colic nearly always implies intrahepatic infection (cholangitis) In acute gall stone attacks leukocytosis of moderate degree is to be expected

ical studies X ray films of the right upper quadrant may reveal calcareous shadows in the region of the gallbladder and less often in the vicinity of the common duct In the absence of such findings cholecystograms should be taken, and the demonstration of calculi in the gallbladder or of a nonfilling gallbladder (carefully checked by a second similar examination) should make a definitive diagnosis In short lived attacks an additional diagnostic



Fig 211 —Calcified gallstones in gall bladder partially filled with dye

*Diagnosis* —The diagnosis of cholelithiasis is nearly always made on the basis of a good history and physical examination The distinguishing feature is the occurrence of episodic attacks of right-upper-quadrant or epigastric pain, with residual tenderness and relative freedom from important symptoms between acute attacks Such a story in an obese individual over the age of forty should immediately lead to a presumptive diagnosis of cholelithiasis and to appropriate radiolog

point may be the demonstration of increased amounts of bilirubin in the serum

*Complications* —Cholangitis or infection of the intrahepatic biliary radicles may occur usually in conjunction with common-duct stones which partially obstruct flow of bile Occasionally though not often cholangitis is associated with obstruction due to calculi in the intrahepatic ducts Perforation of the gallbladder by gall stones with the formation of a biliary fistula into the intestinal

tract has already been mentioned. Impaction of a stone in the ampulla of the cystic duct may be transitory, but if it persists, hydrops of the gallbladder will follow. If unrelieved, eventual infection with empyema of the gallbladder will occur. Partial obstruction of the common duct may persist as a chronic condition and, if unrelieved, may eventually result in early biliary cirrhosis. When obstruction of the common duct is nearly complete and is of long standing, the exclusion of bile from the duodenum may result in the production of hypoprothrombinemia of serious degree. There may be a chronic inflammatory reaction in the common duct, with a resultant stenosis that may make surgical measures extremely difficult and dangerous. In a certain number of instances a gall stone impacted in the ampulla of Vater not only may result in typical obstructive jaundice, but in addition may block the flow of pancreatic secretion to such an extent that an associated pancreatitis that will dominate the entire clinical picture may occur.

*Differential Diagnosis.*—Although the diagnosis of cholelithiasis as the cause of important symptoms is relatively easy, it may be confused with pain caused by duodenal ulcer, disease of the right kidney, pancreatitis or cancer of the pancreas. A still further point of confusion is that gall stones may be found in association with any of these conditions. The pains of lead colic, tabetic crisis, angina abdominalis and other rare conditions such as porphyria and polyarteritis nodosa can be differentiated only with great difficulty from those due to biliary colic. A very important point in differential diagnosis has already been discussed under *Diseases of the Liver*. Acute infectious or toxic hepatitis and, less commonly, cirrhosis of the liver may be characterized by episodes of severe right upper quadrant pain and jaundice. A careful history and physical examination may reveal the presence of intrahepatic disease and provide an adequate explanation for the attack of abdominal pain. Confirmatory evidence may be obtained by proper liver function tests. Under such circumstances an exact diagnosis must be obtained, inasmuch as unnecessary and ill advised surgery in the presence of intrahepatic disease is extremely dangerous and may produce fatal results.

Possibly the most difficult diagnostic problem that exists in relation to the possible existence of gall stones is that of painless jaundice. On occasion progressive jaundice due to stones in the common duct may occur without any accompanying history of pain or discomfort. Under these circumstances gradual enlargement of the liver may occur with accompanying clay-colored stools and deeply bile stained urine. No additional symptoms may be present except for pruritis, but anorexia, loss of weight, nausea and vomiting may accompany the condition. In the complete absence of pain or discomfort, such a situation involves consideration of three important conditions: (1) stone in the common duct, (2) cancer of the head of the pancreas, of the ampulla of Vater or of the common duct, and (3) infectious hepatitis. Absolute certainty as to the diagnosis is not always possible, but certain important diagnostic features require careful attention. A so-called silent stone may underlie the presence of jaundice, but it is rare indeed that a carefully taken history will not reveal minor degrees of indigestion of months or years duration, even if there have been no episodes of colicky pain. The establishment of such a history points strongly to the presence of gall stones rather than to malignancy or intrahepatic infection, which are usually accompanied by symptoms of recent date. Physical examination will reveal intense jaundice in all three conditions. In infectious hepatitis the color of the jaundice is predominantly yellow to orange. In prolonged jaundice due to extra hepatic obstruction, the discoloration tends to be brownish or greenish. Hepatic enlargement may be the same in all three conditions, but in infectious hepatitis generalized liver tenderness is more apt to be present than in the presence of obstruction due to stone or neoplasm. The finding of a nodular liver immediately suggests the possibility of new growth. If it is possible to demonstrate enlargement of the spleen, important evidence has been obtained that is highly suggestive of intrahepatic disease rather than of extrahepatic block. A similar connotation may be given to the appearance

of spider angiomata. A palpable mass separate from the probable location of the gallbladder implies the probability of malignant disease. Of greater importance is the finding of a rounded rather elastic mass lying just below the hepatic border in the *midclavicular line, moving with respiration.* If this mass represents a distended gallbladder, the chances are almost certain that the cause of obstruction is extrahepatic and is due to a carcinomatous block of the common duct near or at the sphincter of Oddi. This is the basis for Courvoisier's law and is based upon the fact that obstruction to the flow of bile sufficient to produce intense jaundice is *capable of distending a normal gallbladder* to the point where it can be palpated. Exceptions to this rule are rare but do occur with the result that the finding of a palpable gallbladder in the presence of deep jaundice may indicate the remote possibility of an obstructing stone in the common duct and may justify exploratory surgery.

Laboratory tests that are helpful in the *evaluation of the problem of painless jaundice* may be considered as follows. In progressive obstruction to the outlet of the common duct by invading neoplasm, bile is usually completely absent from the duodenal contents and the stools and urinary urobilinogen is absent or present only in minimal quantities. In the partial obstruction accompanying stone in the common *duct or intrahepatic disease bile pigments* are demonstrable in the intestinal contents and urobilinogen in the urine is normal or even increased. Intrahepatic disease may be suggested by positive results in cephalin flocculation tests. Moderate elevation in the serum of alkaline phosphatase and cholesterol are typical of partial block due either to stone or to intrahepatic disease. The complete obstruction to the flow of bile caused by neoplasm is typically responsible for high values of alkaline phosphatase and cholesterol in the serum. The finding of occult blood in the stools is not diagnostic but, if persistent and *appreciable in quantity*, points toward a diagnosis of malignancy, particularly if hypoprothrombinemia is not marked. Radiological examination occasionally shows a calculus in the region of the common duct. A barium meal may give evidence of definite deformity of the outline of the first and second portions of the duodenum or of distortion of the mucosal pattern. Such a finding is highly suggestive of pancreatic or ampullary malignancy. A sudden decrease in the intensity of jaundice *may be associated with malignant disease of* the ampulla or with common-duct stone. It is more characteristic of the former and is usually associated with evidences of active bleeding from the upper gastrointestinal tract. This is due to the fact that the invading neoplasm has ulcerated in the region of the sphincter of Oddi. In spite of all of these considerations, a satisfactory explanation for *painless jaundice may be impossible, even* after exhaustive studies. In this event, it is usually wise to prepare the patient for exploratory laparotomy in order to establish a diagnosis and carry out proper treatment before the condition of the patient makes it impossible to do so.

*Treatment.*—The treatment of cholelithiasis should be limited to adequate and *well performed surgical maneuvers.* Any individual in otherwise good health in whom the presence of biliary calculi has been demonstrated should have elective cholecystectomy, with or without exploration of the common duct depending upon the actual condition found at operation. Medical treatment of gall stones has no place in proper therapy. Although it is undoubtedly *true that gall stones may remain* asymptomatic for years and may never result in serious complications, the fact remains that the danger of surgery as it is performed today by skilled operators is definitely less than the risks inherent in a policy of *watchful waiting.* In a small percentage of cases it may be proper to avoid surgery because of the presence of other serious disease. This is particularly true if serious renal or pulmonary disease exists. Heart disease in the absence of heart failure is not a contraindication to surgery. Indeed, many patients with coronary heart disease and angina pectoris also have gall stones which cause occasional attacks of biliary colic. In most instances surgical removal of the gall stones is advisable and frequently results in amelioration of the cardiac symptoms. In obviously *poor risk patients in whom repeated attacks*

of biliary colic have occurred cholecystostomy with removal of the stones may be the procedure of choice When gall stones exist in the presence of diabetes there is little doubt that cholecystectomy is indicated and the procedure may be expected to have a beneficial effect on the progress of the diabetes In uncomplicated cases the actual risk of cholecystectomy, with or without exploration of the common duct is between 2 and 4 per cent Obviously the presence of jaundice and cholangitis increases operative mortality but surgical intervention is important and necessary to prevent further complications

The surgical treatment of the acute gallbladder with biliary colic due to stones may be open to some controversy Most surgeons prefer to operate immediately during the attack if an early diagnosis is made If diagnosis is deferred however, and symptoms of acute or subacute cholecystitis have been present for some days then postponement of operation is advisable until the acute inflammatory process has subsided In this event an operation of election should be planned Exploration of the common duct in the absence of jaundice will depend upon the practice and skill of the individual surgeon In the presence of only one large stone in the gallbladder or in the absence of numerous small stones common-duct exploration may properly be avoided provided manual exploration of the duct does not reveal dilatation or suspicious areas suggesting the presence of intraductal stones If numerous small stones are present particularly if jaundice and/or fever have been present during attacks common-duct exploration should be carried out In cases in which a stone is impacted in the vicinity of the ampulla of Vater a transduodenal approach may be necessary to dislodge the calculus In cases in which jaundice has been present for some time the hemorrhagic tendency due to hypoprothrombinemia must be treated by the adequate administration of parenterally administered vitamin K If the obstruction has not produced any serious hepatic insufficiency normal prothrombin values will be obtained If this is impossible then the use of freshly drawn blood immediately preceding and during the operation may cover this particular lack inasmuch as it provides both prothrombin in normal amounts and accelerator globulin

*Complications of surgery* should be mentioned In spite of careful exploration of the common duct it is occasionally impossible to locate small calculi which may be left behind or which may actually appear from higher levels in the ductal system Under these circumstances there is usually a continuation of attacks of biliary colic with or without jaundice and subsequent re-exploration may be necessary Under these circumstances evidence confirmatory of the existence of biliary calculi or gravel may be obtained by studies of material obtained by duodenal drainage During the operation in some institutions the precaution of making a cholangiogram is taken in order to demonstrate hitherto unfound or unsuspected stones which may then be localized and removed When postoperative drainage of the common duct is considered necessary a cholangiogram should be made before the drainage tube is removed

A second complication of gallbaldder surgery is that of trauma to the common duct This is usually the result of carelessness but it occasionally occurs in spite of all possible precautions When the common duct is traumatized jaundice usually occurs a short time after operation It may be accompanied by fever and pain simulating biliary colic or it may result in the appearance of a biliary fistula usually draining through the operative incision Such an occurrence is extremely unfortunate and almost always necessitates further operation which is always difficult and of unpredictable value Reconstruction of a common duct that has already been damaged by trauma or by stenosis secondary to the inflammatory process surrounding impacted gall stones requires the utmost surgical skill If unsuccessful it invariably leads to biliary cirrhosis

CHOLECYSTITIS —Cholecystitis or inflammation of the gallbladder may be acute or chronic and is usually associated with the presence of biliary calculi It may occur in the absence of gall stones as a result of bacterial invasion The colon bacillus, the typhoid bacillus the pneumococcus the staphylococcus and the streptococcus have

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*Diagnosis.*—In cases in which the patient is examined during a mild attack the demonstration of localized tenderness over the gallbladder area may be sufficient to warrant a definite diagnosis. If fever and leukocytosis are present further important evidence has been obtained. Under these circumstances careful roentgenological studies of the entire gastrointestinal tract are indicated following cholecystography. In the absence of demonstrable abnormalities in the gastrointestinal tract the finding of a nonfunctioning gallbladder will be sufficient to warrant elective surgical intervention. It must be admitted, however, that chronic gallbladder disease falls into somewhat the same category as that of chronic appendicitis and failure to demonstrate clearly abnormal gallbladder function should leave the diagnosis of cholecystitis open to serious doubt.

*Treatment.*—Where the evidence of impaired gallbladder function is clear and there is no proof of other organic disease to be found cholecystectomy is indicated. However it is important to emphasize the fact that removal of a chronically inflamed gallbladder may result in no amelioration of symptoms if gall stones are not present. Indeed a very high percentage of cholecystectomies performed for chronic gallbladder disease do little but leave the patient with an abdominal scar and persisting symptoms. Specific medical measures directed toward improving gallbladder function including the therapeutic use of duodenal drainage are of very dubious value.

BILIARY DYSKINESIA.—This term implies the occurrence of biliary colic due solely to spastic contraction of the sphincter of Oddi in the absence of gall stones or of disease of the gallbladder. Such a cause of attacks of right upper-quadrant colicky pain undoubtedly exists but the exact mechanism is not clear. It may be associated with spasm of the duodenum in the vicinity of the ampulla and in specific instances it may be produced in otherwise normal individuals by the administration of morphine or by balloon distention of the duodenum. Whether spasm of the sphincter of Oddi occurs alone is not absolutely known. Consideration of the existence of such a disturbance is of particular importance in individuals who suffer from recurrent attacks of biliary colic after adequate surgical removal of a diseased gallbladder and biliary calculi in the gallbladder or bile ducts. Under these circumstances it is extremely important to avoid secondary surgery and the diagnosis of biliary dyskinesia may be accepted as an explanation for the patient's symptoms if other evidence of cholelithiasis or inflammation of the bile ducts is lacking.

The validity of such a diagnosis may be strengthened by the performance of certain maneuvers. Attacks of pain may be produced by the use of small doses of morphine. Painful episodes may follow the ingestion of such a substance as egg yolk which theoretically produces spasm of the sphincter of Oddi. The use of nitroglycerine may give prompt relief to spontaneously occurring attacks of pain or to those following the ingestion of fatty substances. If the tip of a duodenal tube is placed in position in the duodenum opposite the sphincter of Oddi pain produced by the ingestion of egg yolk or some similar substance may be promptly relieved by the instillation of a solution of magnesium sulphate. With relief of pain a flow of bile should promptly appear. The diagnosis of biliary dyskinesia should never be accepted until thorough studies have conclusively ruled out the possibility of cholelithiasis or disease of the biliary passages or neighboring structures.

CARCINOMA OF THE GALLBLADDER AND BILE DUCTS.—In nearly every instance tumors of the gallbladder and ducts are carcinomatous in nature. In the gallbladder the histological classification may be that of carcinoma simplex, adenocarcinoma or squamous cell carcinoma. In the ducts the scirrhous type of cancer is most frequently encountered although soft extremely friable polypoid growths may occur within the common duct and may simulate gall stones. Although carcinoma of the gallbladder and bile ducts may occur without obvious cause it is in most instances associated with the presence of gall stones and a chronic inflammatory process of long standing. This point is of the utmost importance inasmuch as it emphasizes the wisdom of proper elective surgical procedures directed toward the removal of gall stones and chronically dis-

been the organisms most often found. Infection by Brucella organisms may be the responsible factor.

*Acute gallbladder infection* may occur in the course of the diseases caused by any of these organisms, or it may be encountered without any specific associated disease.

*Morbid Anatomy.*—The gallbladder is usually distended, and the walls tense. Inflammatory adhesions may be formed with the duodenum, the colon, or the omentum. The mucous membrane is swollen by a catarrhal condition, and, as the process continues, areas of necrosis develop and the villi may become hypertrophied, giving the gallbladder a strawberry appearance. A diffuse phlegmonous process may result, and perforation may occur.

*Symptoms and Signs.*—Severe paroxysmal pain, as a rule, is the first indication of the condition. It is most commonly experienced in the right upper quadrant. It may be epigastric in location or in the region of the appendix. Nausea, vomiting and an elevation of pulse and temperature are present usually, with abdominal distention, muscle spasm, and tenderness over the gallbladder area. The gallbladder may be palpable. Intestinal ileus may occur, with marked distention.

*Diagnosis.*—The diagnosis is usually readily made, but certain points of confusion require comment. During the course of intercurrent infection, such as typhoid fever or pneumonia, the appearance of right upper-quadrant pain and tenderness is highly suggestive of a complicating acute cholecystitis. When no other infectious disease is present, acute cholecystitis may simulate acute appendicitis, acute intestinal obstruction or subacute pancreatitis. The presence of fever and leukocytosis will be common to all of these conditions. Abdominal films will be useful primarily in ruling out acute intestinal obstruction. As a rule, the acuteness of the condition precludes immediate cholecystography or gastrointestinal studies, and the diagnosis must eventually rest upon the ultimate localization of tenderness and muscle spasm in the right upper-quadrant along with other evidences of severe acute infection.

*Treatment.*—In the milder cases, the inflammatory process subsides spontaneously with conservative measures. Recovery may be accelerated by the use of streptomycin, penicillin or similar antibiotic agents. In the severer forms, in which there is definite suppuration or a phlegmonous process in the gallbladder, subsidence of the attack may not occur, and, if improvement is not noted in a relatively short time, surgical intervention is indicated, with cholecystectomy. Occasionally, empyema and perforation of the gallbladder may occur, in which event surgical drainage alone may be the only proper immediate maneuver. In this case elective cholecystectomy should be planned after the acute process has subsided. In the milder cases, after evidence of inflammation has disappeared, cholecystography should be performed, and, if interference with gallbladder function can be demonstrated, elective cholecystectomy is indicated.

*Chronic Cholecystitis.*—Chronic cholecystitis may occur in the absence of gall stones and give rise to numerous episodes of mild right upper-quadrant discomfort and tenderness, along with vague symptoms of indigestion and dyspepsia. It may be present in the carrier state of typhoid fever and may be the result of a low grade, chronic inflammatory process due to enteric organisms or those of the Brucella group. The inflammatory process results in a gradual thickening and fibrosis of the walls of the gallbladder, with loss of the normal mucosal villi and a progressive diminution of contractile and concentrating activity. The gross appearance of the mucosa at times justifies the term "strawberry gallbladder."

The *symptoms* of chronic noncalculous cholecystitis may occur in periodic episodes but more commonly are so vague as to make accurate diagnosis difficult. More often than not, digestive symptoms primarily referred to the epigastrium or right upper quadrant and commonly attributed to chronic cholecystitis are found, on careful scrutiny, to be due to irregular eating habits, to faulty regulation of the bowels, to the excessive use of alcohol, tobacco, tea or coffee, or to fatigue and emotional disturbances.

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cased gallbladders, as a safeguard against the future development of malignant lesions.

*Symptoms and Signs.*—The symptoms of malignant disease of the gallbladder or bile ducts will depend upon two factors: (1) the associated presence of biliary calculi and (2) the actual location of the tumor. Carcinoma of the fundus of the gallbladder eventually causes the appearance of dull, constant pain in the right-upper quadrant, with anorexia, loss of weight and weakness. Physical examination will frequently reveal a tender nodular or globular mass in the region of the gallbladder. Jaundice is a late manifestation. In cases in which the tumor is located in the ampulla of the cystic duct or within the lumen of the hepatic, cystic or common ducts, jaundice appears early and, in the absence of biliary calculi, may be unassociated with colicky pain. Where there is malignant involvement of the bile ducts, obstruction to the flow of bile is nearly always present and is usually accompanied by fever and frequently by chills. Metastasis to the liver is common and may be evident because of hepatic enlargement with nodularity. Ascites occurs in the presence of peritoneal implants. If biliary obstruction is marked, all the clinical and laboratory findings commonly observed in this condition may be present. A greenish tint to the discoloration of the skin is fairly characteristic, due to the formation of biliverdin in the bile ducts as a result of prolonged bile stasis.

*Diagnosis.*—The possibility of carcinomatous involvement of the gallbladder or bile ducts should be suggested by the appearance of the clinical features noted above. The fact that there may be a history of repeated attacks of biliary colic implies the existence of biliary calculi; the progressive nature of the advancing disease in most instances should also suggest the probability of additional malignant involvement. In cases in which the diagnosis is in doubt, three procedures may provide the necessary information. Obviously, exploratory laparotomy offers the surest means of identifying the underlying process. In many cases such a maneuver is undesirable because of the general condition of the patient, and diagnostic information may be obtained either by peritoneoscopy or by aspiration biopsy of the liver. Failure to obtain positive evidence of carcinomatous disease by either of these measures does not exclude the diagnosis of cancer. On infrequent occasions, early carcinoma of the gallbladder or of the bile ducts may be found at the time of surgical intervention directed toward the relief of symptoms secondary to demonstrable cholelithiasis or cholecystitis. Under these circumstances, very radical surgery may properly be performed and is occasionally attended with striking success.

## DISEASES OF THE PANCREAS

General Considerations.—The normal functions of the pancreas depend upon the presence of an internal secretion produced by the islands of Langerhans and an external secretion produced by the acinar tissue. The internal secretion, insulin, plays an essential role in the normal control of carbohydrate metabolism. In conditions in which inflammatory disease has destroyed a sufficient number of islet cells, diabetes mellitus may result. A total pancreatectomy, however, is usually associated with the development of a less intense form of diabetes, as judged by insulin requirements, than that encountered in patients with the spontaneously occurring disease. The external secretion contains several digestive ferments and is collected by a branching system of ducts, ducts which eventually lead into the main pancreatic duct, the duct of Wirsung. This discharges in company with the common bile duct, into the ampulla of Vater. In a certain proportion of cases, the pancreatic and the common bile duct open into the intestine by separate orifices. An accessory pancreatic duct, the duct of Santorini, which opens into the duodenum a little above the duct of Wirsung, is usually present. It also sends a branch to the main duct. The pH of the pancreatic juice is between 7.10 and 8.20. The principal ferments in the pancreatic juice are trypsinogen, pancreatic amylase (amylopsin) and pancreatic lipase (steapsin). Trypsinogen is activated by enterokinase, an enzyme derived from intestinal secretion, and carries the digestion of protein beyond the peptone stage. Unlike pepsin, it is active in an alka-

line medium Pancreatic amylase hydrolyzes starch in much the same manner as salivary amylase but is a much more powerful agent Part of the amylase is believed to be reabsorbed from the intestine In the presence of obstruction to the flow of pancreatic juice it appears in increased quantities in the circulating blood Pancreatic lipase splits the fat molecule into its constituents glycerine and fatty acid The latter combines with alkali to form soaps, which in turn act as an emulsifying agent The secretion of pancreatic juice is under both hormonal and nervous control The latter is mediated over the vagus nerves and produces a secretion that is low in volume but particularly rich in ferments This type of secretion is blocked by the administration of atropine The hormonal control of pancreatic secretion is affected by the action of a substance called secretin derived from the duodenal secretion and produced under the stimulation of acid chyme coming into contact with the duodenal mucosa The action of secretin is not reduced by the administration of atropine The volume of pancreatic external secretion is much greater after stimulation by secretin than after vagal stimulation Marked reduction in the amount of external pancreatic secretion due to pancreatic disease or to the exclusion of pancreatic secretion from the digestive tract, results in diarrhea or the passage of bulky pale stools containing varying amounts of undigested fat protein and starch Even total extirpation of the pancreas does not of necessity produce totally inadequate digestion of foodstuffs inasmuch as the succus entericus may provide sufficient enzyme activity to permit a reasonable degree of alimentation Diseases of the pancreas therefore may result in symptoms referable to hypoinsulinism or to those secondary to inadequate enzymatic digestion of food materials in the upper intestinal tract or to both factors

Pancreatic disease may be due to acute or chronic inflammatory processes to new growths or to cyst formation

PANCREATITIS — *Acute pancreatitis* is due to an inflammatory process produced by a variety of causes It may be the result of obstruction to the flow of external secretion with consequent escape of pancreatic enzymes into the acinar tissue It may be caused by bacterial invasion of the gland Occasionally it occurs as the result of the rupture of a large vessel with sudden hemorrhage into the organ In certain cases hemorrhagic pancreatitis is due to obstruction of the outlet of the ampulla of Vater and the consequent passage of bile into the pancreatic duct system Such an occurrence may be secondary to the presence of a gall stone obstructing the ampulla or to swelling of the sphincter of Oddi or of the adjacent duodenal mucosa (Archibald) According to Dragstedt and his associates only about 60 per cent of the cases of hemorrhagic pancreatitis arise in subjects with chronic biliary tract disease and in only about 10 per cent of these is the ampulla obstructed by a gall stone When a reflux of bile into the pancreas occurs the subsequent rupture of the duct wall and the escape of the pancreatic juice into the interstitial tissue of the pancreas is thought to be the essential factor in the production of the hemorrhagic lesion According to Rich and Duff obstruction to the flow of pancreatic juice may be due to metaplasia of the epithelial lining of a branch of the pancreatic duct within the gland with resultant rupture of a dilated ductule or acinus This is more likely to occur when the secretion pressure of pancreatic juice is high—*i e* after a large meal or the ingestion of alcohol As a result of some form of obstruction to the flow of pancreatic juice, or as a result of actual infection of the pancreatic tissue hemorrhages occur into the glandular substance with necrosis of cells This is accompanied by the escape of lipase *from the disorganized gland with resultant* fat necrosis in the mesentery omentum and peritoneum as well as in the pancreas itself Where hemorrhagic necrosis is extreme a sanguinous fluid is usually found in the peritoneal cavity

*Symptoms and Signs* — The severity of symptoms varies with the degree of involvement of the acinar tissue The onset is usually sudden with excruciating epigastric or upper abdominal pain This pain may radiate to the back usually to the left of the spine Vomiting is a prominent symptom particularly if the attack occurs after a heavy

eased gallbladders, is a safeguard against the future development of malignant lesions.

*Symptoms and Signs.*—The symptoms of malignant disease of the gallbladder or bile ducts will depend upon two factors: (1) the associated presence of biliary calculi and (2) the actual location of the tumor. Carcinoma of the fundus of the gallbladder eventually causes the appearance of dull constant pain in the right upper-quadrant with anorexia, loss of weight and weakness. Physical examination will frequently reveal a tender nodular or globular mass in the region of the gallbladder. Jaundice is a late manifestation. In cases in which the tumor is located in the ampulla of the cystic duct or within the lumen of the hepatic, cystic or common ducts, jaundice appears early and, in the absence of biliary calculi, may be unassociated with colicky pain. Where there is malignant involvement of the bile ducts, obstruction to the flow of bile is nearly always present and is usually accompanied by fever and frequently by chills. Metastasis to the liver is common and may be evident because of hepatic enlargement with nodularity. Ascites occurs in the presence of peritoneal implants. If biliary obstruction is marked, all the clinical and laboratory findings commonly observed in this condition may be present. A greenish tint to the discoloration of the skin is fairly characteristic, due to the formation of biliverdin in the bile ducts as a result of prolonged bile stasis.

*Diagnosis.*—The possibility of carcinomatous involvement of the gallbladder or bile ducts should be suggested by the appearance of the clinical features noted above. The fact that there may be a history of repeated attacks of biliary colic implies the existence of biliary calculi; the progressive nature of the advancing disease, in most instances, should also suggest the probability of additional malignant involvement. In cases in which the diagnosis is in doubt, three procedures may provide the necessary information. Obviously exploratory laparotomy offers the surest means of identifying the underlying process. In many cases such a maneuver is undesirable because of the general condition of the patient and diagnostic information may be obtained either by peritoneoscopy or by aspiration biopsy of the liver. Failure to obtain positive evidence of carcinomatous disease by either of these measures does not exclude the diagnosis of cancer. On infrequent occasions, early carcinoma of the gallbladder or of the bile ducts may be found at the time of surgical intervention directed toward the relief of symptoms secondary to demonstrable cholelithiasis or cholecystitis. Under these circumstances very radical surgery may properly be performed and is occasionally attended with striking success.

## DISEASES OF THE PANCREAS

GENERAL CONSIDERATIONS.—The normal functions of the pancreas depend upon the presence of an internal secretion produced by the islands of Langerhans and an external secretion produced by the acinar tissue. The internal secretion, insulin, plays an essential role in the normal control of carbohydrate metabolism. In conditions in which inflammatory disease has destroyed a sufficient number of islet cells, diabetes mellitus may result. A total pancreatectomy, however, is usually associated with the development of a less intense form of diabetes, as judged by insulin requirements, than that encountered in patients with the spontaneously occurring disease. The external secretion contains several digestive ferments and is collected by a branching system of ducts, ducts which eventually lead into the main pancreatic duct, the duct of Wirsung. This discharges, in company with the common bile duct, into the ampulla of Vater. In a certain proportion of cases the pancreatic and the common bile duct open into the intestine by separate orifices. An accessory pancreatic duct, the duct of Santorini, which opens into the duodenum a little above the duct of Wirsung, is usually present. It also sends a branch to the main duct. The pH of the pancreatic juice is between 7.10 and 8.20. The principal ferments in the pancreatic juice are trypsinogen, pancreatic amylase (amylopsin) and pancreatic lipase (steapsin). Trypsinogen is activated by enterokinase, an enzyme derived from intestinal secretion, and carries the digestion of protein beyond the peptone stage. Unlike pepsin, it is active in an alka-

the inflammatory process may alter the external secretion to a degree sufficient to cause the formation of small calculi which may obstruct the small ducts or even become impacted in the duct of Wirsung with accompanying obstruction to the flow of pancreatic juice and as a result pain The degree of fibrosis and degeneration present in a given gland will determine the character of the symptoms

*Symptoms and Signs* —Where extensive degeneration and fibrosis have occurred the patient complains of alteration of bowel habits and a change in the character of the stools Frank diarrhea may occur but more often the condition is characterized by the frequent passage of bulky or frothy grayish or light yellow stools that glisten because of the high fat content They are usually extremely foul Weight loss may be a striking feature and a certain degree of malnutrition is invariably present Pain may be entirely lacking but when present is usually epigastric in location with radiation through to the back It is usually brought on by the ingsetion of food containing appreciable quantities of fats or proteins Alcohol in excess also initiates attacks of pain Jaundice is a variable feature and usually depends on whether the head of the pancreas is involved by a fibrosing process in close proximity to the ampulla of Vater The jaundice may be due however to the associated presence of biliary calculi Diabetes mellitus with glycosuria may be present but is by no means a constant accompaniment of the condition Physical examination reveals general malnutrition During episodes of pain tenderness over the area of the entire pancreas can usually be demonstrated

*Diagnosis* —A history of gradually increasing change in bowel activity with the passage of fatty stools and an accompanying loss of weight should suggest the possibility of chronic pancreatitis The occurrence of epigastric pain with radiation into the back occurring after the intake of food or alcohol is further important diagnostic evidence Laboratory measures are limited Where chronic pancreatitis is accompanied by severe attacks of pain one may expect to find an elevation of serum amylase It should be remembered however that progressive destruction of the gland may reduce the production of pancreatic amylase to a point where elevated values in the serum may not be possible In the absence of this specific test determinations of pancreatic enzyme activity either by microscopic examination of the stools or by study of the duodenal contents may give a clue to the underlying process In advanced cases the stools will invariably show excessive amounts of fat or fatty acid and the presence of numerous undigested muscle fibers provided the patient is taking appreciable quantities of fatty substances and red meat Analysis of the duodenal contents for enzyme determinations requires special laboratory techniques The flow of pancreatic juice may be stimulated by the administration of secretin or cholinergic drugs or by the ingestion of a fatty meal or a meal containing peptones An experienced technician may be able to demonstrate levels of enzyme activity far below those encountered in normal individuals A film of the upper abdomen is frequently of great help in demonstrating disseminated calcification of the pancreas or in suggesting the presence of pancreatic calculi

*Treatment* —When pain is not a prominent feature essential treatment consists primarily in the use of potent pancreatic extracts These are now available and contain adequate amounts of potent proteolytic lipolytic and amylolytic enzymes which may be administered with the meals The use of these preparations is at times accompanied by improvement in intestinal absorption with modification of the stools and a reduction in the degree of intestinal flatulence The addition of an emulsifying agent such as Tween-80 may increase fat absorption It is rarely possible to correct completely the deficiency in pancreatic enzyme activity When diabetes is present it should be treated according to the general principles embodied in the therapy of this disease In cases in which pain is an important feature the therapeutic problem is a complicated one inasmuch as these patients tend to become addicted to the use of morphine or its derivatives or to the excessive use of alcohol which at times relieves abdominal discomfort

meal or the excessive intake of alcohol. Epigastric tenderness is almost invariably present, and, where extensive necrosis exists, the tenderness may extend well to the left of the midline, going over to the region over the tail of the pancreas. Left costovertebral angle tenderness may occur. In severe cases symptoms of shock are marked, with rapid pulse, low blood pressure and extreme pallor or cyanosis. Fever is almost invariably present except in the mildest cases. Jaundice may be present but is usually of only moderate intensity. The patient may die within a few hours of the onset of the disease, but usually the course of the disease covers a period of several days or weeks. In serious cases the progress of the disease may be marked by electrolyte loss and dehydration, the appearance of ascites and occasionally the signs of frank tetany.

*Diagnosis* usually is made on the basis of an acute fulminating attack and physical signs. The condition must be differentiated from perforation of a gastric or duodenal ulcer, acute cholecystitis, intestinal obstruction and acute peritonitis with rupture. Coronary thrombosis may simulate an acute hemorrhagic pancreatitis and occasionally the condition is confused with diaphragmatic pleurisy and pneumonia. In acute hemorrhagic pancreatitis muscle rigidity may be encountered, but it is much less marked than that associated with a perforated viscus. Abdominal tenderness is more in the midline or to the left of the midline than that commonly encountered in acute cholecystitis. An attack of coronary thrombosis may be associated with severe abdominal pain, but a careful history will usually elicit a previous story of angina pectoris or exertional dyspnea. Abdominal films to exclude the presence of gas under the diaphragm will be helpful in deciding against the diagnosis of a perforated ulcer. The white blood cell count in acute hemorrhagic pancreatitis usually reaches a very high level, but this in itself is not diagnostic. The most important single laboratory test is the determination of serum amylase. During the acute stage of the disease serum amylase values may be several times the normal value and in most instances such a findin is practically diagnostic of the condition. Amylase values may fall rapidly as the attack progresses. Therefore, several early determinations are important.

*Treatment.*—In recent years conservative therapy has been strongly advocated because of the high mortality rate attending earlier operative procedures and because of the fact that a very large number of patients with acute pancreatitis recover spontaneously. Initial measures should include the parenteral administration of adequate amounts of fluid and electrolytes. In the presence of shock whole-blood transfusions or the use of plasma when blood is not immediately available may be a life saving procedure. Oral feeding should be avoided at least in the early stages of the disease. Absolute bed rest and the use of sufficient quantities of morphine to relieve pain are essential. If the course of the disease suggests a suppurative process antibiotic therapy should be employed, and when tetany is present due to a striking lowering of the blood calcium the intravenous administration of calcium gluconate is an important measure. In the presence of shock surgery should be avoided, but with general improvement in the condition of the patient surgical intervention may be proper if there are evidences of spreading peritonitis or increasing icterus. Surgical maneuvers should be limited to cholecystostomy and simple drainage. A late complication of the disease may be that of abscess formation due to local suppuration. When this complication occurs surgical drainage is necessary. If gall stones are demonstrated after the attack has subsided proper elective surgical measures should be planned.

*Prognosis.*—The mortality rate for this condition ranges between 10 and 30 per cent. Recurrences of the condition may occur especially if biliary calculi are present in the common duct.

Chronic Pancreatitis.—Chronic pancreatitis is difficult to diagnose with any degree of consistency. The disease is usually the result of chronic or recurrent inflammation of the gland with consequent degeneration of pancreatic tissue and fibrosis. The degenerative process may be associated with extensive areas of calcification indicative of previous hemorrhage or necrosis. At times

the inflammatory process may alter the external secretion to a degree sufficient to cause the formation of small calculi which may obstruct the small ducts or even become impacted in the duct of Wirsung with accompanying obstruction to the flow of pancreatic juice and as a result pain The degree of fibrosis and degeneration present in a given gland will determine the character of the symptoms

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*Treatment* —When pain is not a prominent feature essential treatment consists primarily in the use of potent pancreatic extracts These are now available and contain adequate amounts of potent proteolytic lipolytic and amylolytic enzymes which may be administered with the meals The use of these preparations is at times accompanied by improvement in intestinal absorption with modification of the stools and a reduction in the degree of intestinal flatulence The addition of an emulsifying agent such as Tween 80 may increase fat absorption It is rarely possible to correct completely the deficiency in pancreatic enzyme activity When diabetes is present it should be treated according to the general principles embodied in the therapy of this disease In cases in which pain is an important feature the therapeutic problem is a complicated one inasmuch as these patients tend to become addicted to the use of morphine or its derivatives or to the excessive use of alcohol which at times relieves abdominal discomfort

When the problem of intractable pain is present, surgical intervention is frequently indicated. Two major surgical maneuvers require consideration. Total pancreatectomy may be performed. Such a radical procedure is justified only in extreme cases and should be avoided, if possible, because of the undesirable side effects. The resultant diabetes must be taken care of and the dietary and medicinal measures necessary to maintain nutrition are very complicated.

*Morbid Anatomy.*—The characteristic lesion is a widespread change in the mucus secreting glands of the entire body. The striking findings in the pancreas are but one manifestation. In the pancreas, initially, dilatation of the acini and the ducts is followed by atrophy of the acinar tissue. This tissue is replaced with connective tissue and ultimately, there is widespread fibrosis. Striking changes are characteristically found in the lungs and in the acini and the ducts of



FIG. 212.—Calcification of pancreas (head) with one large calculus in duct of Wirsung.

An entirely different maneuver which may give adequate symptomatic relief is that of splanchnicectomy. A left splanchnicectomy occasionally gives complete relief from pain but, in some instances, bilateral section of the sensory pathways may have to be performed.

CYSTIC FIBROSIS OF THE PANCREAS is a familial congenital disease characterized by steatorrhea due to insufficiency of the external secretion of the pancreas. It is associated with chronic bronchitis, bronchiolitis, recurrent bronchopneumonia and bronchiectasis. The disease is uncommon but may occur in more than one member of a family.

the salivary glands, and fatty infiltration of the liver is usually present.

*Clinical manifestations* are usually those of nutritional disturbances secondary to grossly deficient or absent pancreatic enzymes. Foul bulky stools appear early in infancy and in children afflicted with the condition who survive the first six months of life emaciation is extreme. About half the infants die of associated pulmonary infection secondary to widespread bronchiolar obstruction by thick tenacious mucus. The longest recorded survival is 14½ years.

*Diagnosis* of the condition is based upon recognition of symptoms secondary to pancreatic insufficiency in combination with

chronic pulmonary disease Examination of the stools reveals obvious steatorrhea and nitrogen loss Vitamin A absorption curves demonstrate poor absorption of the vitamin Roentgenological studies of the gastrointestinal tract are not diagnostic but show the changes characteristic of deficiency disease

*Treatment* consists in the administration of potent pancreatic extract in adequate *amounts plus a well balanced diet* The use of vitamin A preparations may be of extreme importance in growing children and, at times it may be necessary to combat hypo-

The *diagnosis* of islet-cell tumor is based on the occurrence of repeated episodes of typical spontaneous hypoglycemia These attacks must be differentiated from those occurring as a result of hepatic disease hypopituitarism adrenal-cortical insufficiency, and hypothyroidism as well as from those without demonstrable anatomical lesions classified as functional hypoglycemia

*Treatment* consists in surgical removal of the tumor or tumors and in most instances is eminently successful (*See* Chapter 15)

MALIGNANT TUMORS of the pancreas are practically always carcinomatous and arise



FIG 213 —Carcinoma of the head of the pancreas removed surgically An applicator is inserted in the common bile duct (Herbut s Surgical Pathology )

thrombinemia secondary to diminished absorption of fat soluble vitamin K Measures directed toward the prevention or care of pulmonary infection are obviously necessary

TUMORS OF THE PANCREAS —Both benign and malignant tumors of the pancreas are encountered The former are practically always benign adenomas of islet cells and symptoms are essentially due to hyperinsulinism with the production of hypoglycemic attacks Occasionally metastases may occur but they are unusual Islet tumors occur *most frequently in the body or tail of the* pancreas and are often multiple

from the acinar or duct epithelium Pancreatic cancer is extremely common and is *most frequently found in the head of the organ* It occurs very much more frequently in men than in women and is usually encountered in the later decades of life There may be an increased incidence of this condition in diabetic patients and it is not infrequently associated with the presence of gall stones

*Symptoms and Signs* —The symptoms and physical signs of cancer of the pancreas depend largely on the exact location of the lesion When cancer occurs in the tail or body of the organ there may be no symptoms until metastases occur In cancer of

the body of the pancreas pain is commonly encountered, due either to more or less accompanying obstruction of the main pancreatic duct or to involvement of the celiac plexus The pain is usually described as a deep steady boring discomfort It seems to originate in the epigastrium and typically radiates posteriorly to the back in the left lower thoracic region or in the interscapular area When severe it is relieved only by the hypodermic use of morphine or similar drugs Cancer of the head of the pancreas is typically accompanied by the gradual onset of gross evidence of increased amounts of fat A palpable mass may be present and in advanced cases, metastases to the liver may be evidenced by the finding of hepatic enlargement with nodularity

*Diagnosis* —Diagnosis of cancer of the tail or body of the pancreas must be made on purely clinical grounds Diagnosis of cancer of the head of the pancreas must be differentiated from cancer of the ampulla of Vater or common bile duct and from biliary obstruction due to stone in the common duct Many of the differential points have already



Fig 214 —Carcinoma of the head of the pancreas Note the displacement of the duodenal loop and the pressure on the greater curvature of the stomach (Portis Diseases of the Digestive System )

jaundice, which increases steadily until the patient is deeply pigmented Itching may be present and at times is intolerable Pain is a frequent accompaniment of the condition and is usually steady and boring in character The presence of gall stones is not uncommon and this fact may modify the picture because of episodes of colicky pain Loss of weight may be marked and both loss of appetite and actual distaste for food are commmon Increased frequency of bowel movements may occur, and the stools frequently show been discussed in detail under *painless jaundice* Direct evidence of carcinomatous involvement of the head of the pancreas may be obtained by the use of a barium meal with demonstrable deformity or alteration in the mucosal pattern of the first and second portions of the duodenum

*Treatment* —Treatment of cancer of the pancreas is limited to surgical procedures In spite of the brilliant operative results obtained by Whipple and others it is still true that a successful surgical cure of this

condition is extremely uncommon This is largely due to two factors first the diagnosis is usually not made until the disease is well advanced second metastases to regional lymph nodes the thoracic duct and adjacent blood vessels render adequate surgery almost impossible Total pancreatectomy is a formidable procedure but has been successfully accomplished in a number of instances It should be attempted only when the patient is in reasonably good physical condition and when the services of an unusually competent surgeon are available When such a radical procedure is not advisable palliative measures will be of help in the temporary elimination of jaundice and itching This may be accomplished by the external biliary drainage of the dilated common duct or by the performance of a cholecystgastrostomy or cholecyst-enterostomy Survival after any of these surgical procedures however is usually short

CYSTS OF THE PANCREAS —The most common cysts of the pancreas are classified as pseudocysts and are the result of trauma or inflammation of the organ They develop outside the body of the pancreas and do not contain pancreatic enzymes True cysts of the pancreas may result from obstruction to the main duct or its tributaries or may occur following a hemorrhagic or necrotizing process in the body of the gland Parasitic cysts are rare Proliferation cysts are usually associated with tumor formation Retention cysts and proliferation cysts usually contain active pancreatic enzymes

*Symptoms* —The symptoms obviously depend upon the location of individual cysts and the rapidity with which they develop Pseudocysts usually develop rapidly following severe trauma to the epigastrium or an acute attack of pancreatitis Epigastric swelling develops rapidly with a sensation of fullness and tension Pain may be present The development of other types of pancreatic cysts is more gradual and is usually not accompanied by pain unless there is hemorrhage into the cystic area If cystic involvement of the pancreas is associated with malignant disease the symptoms of loss of weight and malignant cachexia will be present

*Diagnosis* —The cystic mass may be readily palpable as a spheroid tumor that is not excessively hard It may increase in size till it is readily visible Roentgenological examination will usually provide information leading to a reasonably exact diagnosis Barium meal will show the tumor mass to be outside the stomach the duodenum or the upper small bowel At times a barium enema may be necessary to provide evidence that the tumor is external to the transverse colon Abdominal films will usually demonstrate a rounded or lobular radio-opaque mass Intravenous pyelograms may be necessary to rule out left renal tumor

*Treatment* —When symptoms are present or the cystic tumor is steadily increasing in size surgical intervention is necessary Excision of unilocular cysts may be possible but this is not always the case Marsupialization is frequently necessary When this is performed continued suction must be carried out until sclerosing solutions can be used to stop active secretion by the lining cells A persistent fistula can be transplanted successfully into the stomach or the adjacent small bowel

## REFERENCES


*General*

POCKES H I Gastro-Enterology Philadelphia W B Saunders Company 1944 *I III*

GOLDEN R Diagnostic Roentgenology New York Thomas Nelson and Sons 1950

*Pain*

JONES C M Digestive Tract Pain New York Macmillan Company 1938

*Nutrition*

SPIES T D and BUTT H R Vitamins and Avitaminosis in Duncan G G Diseases of Metabolism 2nd ed Philadelphia W B Saunders Company 1947

SYDENSTRICKER V P The Clinical Manifestations of Nicotinic Acid and Riboflavin Deficiency (Pellagra) Ann Int Med 1941 *14* 1499

YOUMANS J B Nutritional Deficiencies Philadelphia J B Lippincott Company 1941

Metabolism During Convalescence Prepared under the direction of the Committee on Convalescence and Rehabilitation of the National Research Council War Medicine 1944 *6* 1

WOHL Michael G Dietotherapy Gastrointestinal Diseases Clinical Nutrition edited by Joliffe Norman, M D Tisdall F F M D, and Cannon Paul R M D Paul C Hoeber Inc, 1950 640-655

*Esophagus*

BENEDICT E B and SWEET R H Benign Stricture of the Esophagus Gastroenterology 1948 *11* 618

CHAMBERLAIN D T Peptic Ulcer of the Esophagus Am J Dig Dis 1939 *6* 725

HARRINGTON S W Pulsion Diverticulum of the Hypopharynx at the *Pharyngo-Esophageal* Junction Surgery 1945 *18* 66

HURST A F and RAKE G W Achalasia of the Cardia (So-Called Cardiospasm) Quart J Med 1930 *23* 491

JONES C M Hiatus Esophageal Hernia New Eng J Med 1941 *225* 963

KAMPMEIER R H and JONES F Esophageal Obstruction Due to Gummata of the Esophagus and Diaphragm Am J Med Sc 1941 *201* 539

LOCKARD L B Esophageal Tuberculosis Laryngoscope 1938 *23* 561

SWEET R H Treatment of Cancer of the Esophagus Surgery 1948 *23* 952

*Stomach*

*Pyloric Stenosis*

BERK L and DUNLAP H J Hypertrophic Pyloric Stenosis in Adults Ann Surgery 1944 *119* 124

VANCE C A Congenital Pyloric Stenosis Ann Surgery 1944 *119* 351

WAKEFIELD H Hypertrophic Pyloric Stenosis in Adults Gastroenterology 1944 *2* 250

*Gastritis*

BEAUMONT W Experiments and Observations on the Gastric Juice and the Physiology of Digestion Plattsburg F P Allen 1833

CLAGETT O T and WALTERS W Tuberculosis of the Stomach Arch Surg 1938 *37* 505

FINDLEY J W JR KIRSNER J B PALMER W L and PULLMAN T N Chronic Gastritis Am J Med 1949 7 198

JONES C M BENEDICT, E B and HAMPTON A O Variations in the Gastric Mucosa in Pernicious Anemia *Am J Med Sci* 1935 *190* 596

PATTERSON C O and ROUSE M O Description of Gastroscopic Appearance of Luetic Gastric Lesions in Late Acquired Syphilis Gastroenterology 1948 *10* 474

SCHINDLER R Gastroscopy The Endoscopic Study of Gastric Pathology Chicago University of Chicago Press Revised 1949

WOLF S and WOLFF H G Human Gastric Function the *Experimental* Study of a Man and His Stomach New York Oxford University Press 1943

*Peptic Ulcer*

ALVAREZ W C Chapter on Hunger Contraction *and the Pain of Ulcer* An Introduction to Gastroenterology New York P B Hoeber Inc 1939

BONNEY G L W and PICKERING G W Observations on the Mechanism of Pain in Ulcer of *the Stomach and Duodenum I The Nature of* the Stimulus II The Location of the Pain Nerve Endings Clinical Science 1946 *6* 65 91

CULVER P J The Dumping Syndrome Medical Clinics of North America 1949 *33* 1321

DRAGSTEDT L R HARPER P V TOVEE F B and WOODWARD E R Section of the Vagus Nerves of the Stomach in the Treatment of Peptic Ulcer Complications and Results after Four Years Ann Surgery 1947 *126* 687

EMERY E S JR The Treatment of Peptic Ulcer Based on 1435 Cases Am J Digest Dis 1934 *1* 520

HAMPTON A O Safe Method for Roentgen Demonstration of Bleeding Duodenal Ulcers Am J Roent 1937 *38* 565

HURST A F and STEWART J Gastric and Duodenal Ulcer London Oxford University Press 1929

JONES C M Medical and Surgical Treatment of *Peptic Ulcer Bull New York Acad Med* 1949 *25* 488

——— Nutritional Aspects of Anastomotic Operations California Medicine 1949 *71* 253

JONES C M CULVER P J DRUMMEY G H and RYAN A E *Modification of Fat Absorption* in the Digestive Tract by the Use of an Emulsifying Agent Ann Int Med 1948 *29* 1

KONJETZNY G E Die Entzundliche Grundlage der Typischen Geschwursbildung im Magen unt Duodenum Berlin Julius Springer 1930

McKITTRICK L S and MOORE F D Complications and Mortality in Subtotal Gastrectomy for Duodenal Ulcer Ann Surgery 1944 *120* 531

MAGE S Recurrence of Ulceration Following Subtotal Gastrectomy in the Treatment of Gastroduodenal Ulcer Ann Surgery 1942 *116* 729

PALMER W L Mechanism of Pain in Gastric and Duodenal Ulcers Arch Int Med 1926 *38* 603 1926 *38* 694 1927 *39* 109

PALMER W L and HEINZ T E Mechanisms of Pain in Gastric and Duodenal Ulcers Arch Int Med 1934 *53* 269

RICKETTS W S PALMER W L KIRSNER J D and HAMANN A Radiation Therapy and Peptic Ulcer Gastroenterology 1948 *11* 789

WINKELSTEIN A A New Therapy for Peptic Ulcer Continuous Alkalinized Milk Drip into the Stomach Am J *Med Sci* 1933 *185* 699

WOLLAGER F F COMFORT M W and WEIR J F I The Total Solids Fat and Nitrogen in the Feces II Study of Persons who had Undergone Partial Gastrectomy with Anastomosis of Entire Cut End of Stomach and Jejunum (Polya Anastomosis) Gastroenterology 1946 *6* 93

Pain Proceedings of the Association for Research in Nervous and Mental Disease New York Williams & Wilkins Company 1943 Chapters XX XXI XXII

*Cancer and Ulcer*

BENEDICT E B Differential Diagnosis of Benign and Malignant Lesions of the Stomach by Means of the Flexible Operating Gastroscope Gastroenterology 1950 *14* 275

CAREY J B and HAY I Gastric Polyps Gastroenterology 1948 *10* 102

RIGLER L and KAPLAN H Pernicious Anemia and Tumors of the Stomach J Nat Cancer Inst 1947 7 327

STOUT A I Gastric Mucosal Atrophy and Carcinoma of the Stomach New York State J Med 1945 *4* 973

ULFELDER H GRAHAM R and MEIGS J V Further Studies of Cytologic Method in Problems of Gastric Cancer Ann Surgery 1948 *128* 422

WALTERS W GRAY H K and PRIESTLY J T Carcinoma and other Malignant Lesions of the Stomach Philadelphia W B Saunders Company 1942

WELCH C F and ALLEN A W Carcinoma of the Stomach New England J Med 1948 238 583

*Small Intestine*

HOWELL L M Meckel's Diverticulum A Consideration of the Anomaly with a Review of 61 Cases Am J Dis Children 1946 *71* 365

MOSES W R Meckel's Diverticulum New England J Med 1947 *237* 118

*Tumors*

BOCKUS H L Tumors of the Small Intestine in Gastro-Enterology Philadelphia W B Saunders Company 1944 *2* 124

*Inflamatory Disease*

BROWN I and SAMPSON H L Intestinal Tuberculosis 2nd Ed Philadelphia Lea & Febiger 1930

CULLEN J H Intestinal Tuberculosis Clinical Pathological Study Quart Bul Sea View Hospital 1940 *5* 143

*Regional Enteritis*

COMBE C and SAUNDERS W A Singular Case of Stricture and Thickening of the Ileum Case Report Presented Before Royal College of Physicians in London July 1806 London Medical Transactions College of Physicians 1813 *4* 16

CROHN B B Regional Ileitis New York Grune & Stratton 1949

CROHN B B and ROSENAK B D A Combined Form of Ileitis and Colitis J A M A 1936 *106* 1

GARLOCK J H and CROHN B B An Appraisal of the Results of Surgery in the Treatment of Regional Ileitis J A M A 1945 *127* 205

*Appendicitis*

FITZ R H Perforating Inflammation of the Vermiform Appendix Am J Med Sci 1886 *92* 321

REYNOLDS J T Appendicitis Basic Considerations in Choice of Therapy S Clin No America 1944 *24* 128

WAGENSTEEN O H and BOWERS W T Significance of Obstructive Factor in Genesis of Acute Appendicitis Experimental Study Arch Surg 1937 *34* 496

*Large Intestine*

*Mucous Colitis*

ALVAREZ W C An Introduction to Gastroenterology New York Paul B Hoeber Inc 1948

BOCKUS H L and BANK J C Mucous Colitis a Cyclopedia of Medicine Surgery and Specialties Philadelphia F A Davis Company 1939 *4* 368

DACOSTA J M Mucous Enteritis Am J Med Sci 1871 *89* 321

FRIEDENWALD J FELDMAN M and ROSENTHAL L J Mucous Colitis Observations in 500 Cases Ann Int Med 1929 *3* 521

JORDON S M and KIEFFER E D Irritable Colon J A M A 1929 *93* 592

WHITE B V COBB S and JONES C M Mucous Colitis A Psychological Medical Study of Sixty Cases Psychosomatic Medicine Monograph 1 1939

*Megacolon*

BOSWORTH B M STEIN H D and LISA J R Modern Management of Megacolon Am J Surg 1948 75 808

SWENSON O and BILL A H JR Resection of Rectum and Rectal Sigmoid with Preservation of Sphincter for Benign Spastic Lesions Producing Megacolon Experimental Study Surgery 1948 *24* 212

SWENSON O RHEINLANDER H F and DIAMOND I Hirschsprung's Disease A New Concept of Etiology Operative Results in 34 Patients New England J Med 1949 *241* 551

*Diverticulitis*

BLIE L A Diverticula of the Colon New England J Med 1939 *221* 593

ERDMANN J F Diverticulitis New England J Med 1940 *223* 846

LEROYER C P and WHITE B V Diagnostic and Therapeutic Problems in Diverticulitis New England J Med 1948 *239* 245

MORTON J J JR Diverticulitis of the Colon Ann Surgery 1946 *124* 725

*Tumors*

BERK J E in Bockus H L Gastro-Enterology Philadelphia W B Saunders Company 1944 *2* 711 788

ERDMANN J F and MORRIS J H Polyposis of the Colon A Survey of the Subject Sur Gyn Obst 1925 *40* 460

MAYO C W Malignant Lesions of the Right Portion of the Colon Proc Staff Meet Mayo Clinic 1941 *16* 67

*OCHSNER A and MAHORNER H in Pack G T* and Livingston E M Treatment of Cancer and Allied Diseases New York Paul B Hoeber Inc 1940

RAIFORD T S Carcinoid Tumors of the Gastrointestinal Tract (So-Called Argentaffin Tumors) Am J Cancer 1933 *18* 803

RANKIN F W BARGEN J A and BUIE L A The Colon Rectum and Anus Philadelphia W B Saunders Company 1932

RANKIN F W and JOHNSTON C C Cancer of the Colon Chapter XI in Portis S A Diseases of the Digestive System Philadelphia Lea & Febiger 1941

*Ulcerative Colitis*

BARGEN J A The Modern Management of Colitis Springfield Illinois Charles C Thomas 1944

BOCKUS H L Gastro-Enterology Philadelphia W B Saunders Company 1944 *Vol 2* Chapter LXII

CATTELL R B The Surgical Treatment of Ulcerative Colitis Gastroenterology 1948 *10* 63

DANIELS G E Psychiatric Factors in Ulcerative Colitis Gastroenterology 1948 *10* 59

GINSBERG R S and IVY A C The Etiology of Ulcerative Colitis An Analytical Review of the Literature Gastroenterology 1946 *7* 67

LINDEMANN E Modifications in the Course of Ulcerative Colitis in Relationship to Changes in Life Situations and Reaction Patterns Life Stress and Bodily Disease Proceedings of the Association for Research in Nervous and Mental Diseases Williams & Wilkins 1950 *29* 706

MCKITTRICK L S MOORE F D and WARREN R Ulcerative Colitis Ileostomy Problem or Solution? J A M A 1949 *139* 201

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*Liver Physiology*

BEST C H and TAYLOR N B The Physiological Basis for Medical Practice Baltimore The Williams & Wilkins Company 1950

RICH A R The Pathogenesis of the Forms of Jaundice Bull Johns Hopkins Hosp 1930 *47* 338

*Tests of Hepatic Function*

DUCCI H and WATSON C J The Quantitative Determination of the Serum Bilirubin with Special Reference to the Prompt Reacting and the Chloroform-Soluble Types J Lab & Clin Med 1945 *30* 293

HAWKINSON V WATSON C J and TURNER R H Modification of Harrison s Test for Bilirubin in the Urine J A M A 1945 *129* 514

IVERSEN P and ROHOLM K An Aspiration Biopsy of the Liver with Remarks on its Diagnostic Significance Acta Med Scandinav 1939 *102* 1

KUNKEL H G AHRENS E H JR and EISENMENGER W J Application of Turbimetric Methods for Estimation of Gamma Globulin and Total Lipid to Study of Patients with Liver Disease Gastroenterology 1948 *11* 499

MACLAGAN N F The Thymol Turbidity Test as an Indicator of Liver Dysfunction Brit J Exper Path 1944 *25* 234

MATEER J G BALTZ, J I MARION D F and MACMILLAN J M Liver Function Tests J A M A 1943 *121* 723

WATSON C J SCHWARTZ S SBOROV S and BERTIE E Studies of Urobilinogen V A Simple Method for the Quantitative Recording of the Ehrlich Reaction as Carried Out With Urine and Feces Am J Clin Path 1944 *14* 605

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FINDLAY G M and MACCALLUM F O Hepatitis and Jaundice Associated with Immunization against Certain Virus Diseases Proc Roy Soc Med 1938 *31* 779

HANGER F M and GUTMAN A B Post Arsphenamine Jaundice Apparently Due to Obstruction of Intra Hepatic Biliary Tract J A M A 1940 *115* 263

OTTENBERG R and SPIEGEL R Present Status of Non obstructive Jaundice Due to Infections and Chemical Agents Causative Agents *Pathogenesis Inter Relationships* Clinical Characteristics Medicine 1943 *22* 27

WEIR J F and COMFORT M W Toxic Cirrhosis Caused by Cinchophen Arch Int Med 1933 *52* 685

WILSON J D and GOODPASTURE E W Yellow Atrophy of the Liver Acute Subacute and Healed Arch Int Med 1927 *40* 377

*Viral Hepatitis*

BARKER M H CAPPS R B and ALLEN F W Hepatitis in the Mediterranean Theatre J A M A 1945 *128* 997 *129* 653

HAVENS W P JR Infectious Hepatitis Medicine 1948 *27* 279

JONES C M and MINOT G R Infectious (Catarrhal) Jaundice An Attempt to Establish a Clinical Entity Boston Med and Surg J 1923 *189* 531

LUCKÉ B I The Pathology of Fatal Epidemic Hepatitis II The Structure of the Liver in Recovery from Epidemic Hepatitis Am J Path 1944 *20* 471

MALLORY T B The Pathology of Epidemic Hepatitis J A M A 1947 *134* 655

NEEFE J R STOKES J JR REINHOLD J G and LUKENS F D W Hepatitis Due to the Injection of Homologous Blood Products in Human Volunteers J Clin Investigation 1944 *23* 836

NEEFE J R Recent Advances in the Knowledge of Virus Hepatitis M Clin North America 1946 *30* 1407

ROHOLM K and IVERSEN P Changes in the Liver in Acute Epidemic Hepatitis (Catarrhal Jaundice) Based on 38 Aspiration Biopsies Acta Path and Microbiol Scandinav 1939 *16* 427

STOKES J JR and NEEFE J R The Prevention and Attentuation of Infectious Hepatitis by Gamma Globulin J A M A 1945 *127* 144

*Chronic Diseases of the Liver (Cirrhosis)*

BLAKEMORE A H and LORD J W JR The Technic of Using Vitallium Tubes in Establishing Portocaval Shunts for Portal Hypertension Ann Surg 1945 *122* 476

CHAIKOFF I L EICHORN K B CONNON C L and ENTERRMAN C The Production of Cirrhosis in the Liver of the Normal Dog by Prolonged Feeding of a High Fat Diet Am J Path 1943 *19* 9

CHALMERS T C and DAVIDSON C S A Survey of Recent Therapeutic Measures in Cirrhosis of the Liver New England J Med 1949 *240* 449

FLEMING R G and SNELL A M Portal Cirrhosis with Ascites An Analysis of 200 Cases with Special Reference to Prognosis and Treatment Am J Digest Dis 1942 *9* 115

GIBSON W R and ROBERTSON H E So-Called Biliary Cirrhosis Arch Path 1939 *28* 37

GILLMAN T and GILLMAN J Hepatic Damage in Infantile Pellagra and Its Response to Vitamin Liver and Dried Stomach Therapy as Determined by Repeated Liver Biopsies J A M A 1945 *129* 12

GILLMAN T MANDELSTAM J and GILBERT C Production of Severe Hepatic Injury in Rats by Prolonged Feeding of Maize-meal Porridge (Mealie-Pap) and Sour Milk Brit J Exper Path 1945 *26* 67

GYORGY P Experimental Hepatic Injury Am J Clin Path 1944 *14* 67

GYORGY P and GOLDBLATT H Treatment of Experimental Dietary Cirrhosis of the Liver in Rats J Exper Med 1949 *90* 73

HIMSWORTH H P The Liver and Its Diseases Cambridge Harvard University Press 1947

JONES C M and VOLWILER W Therapeutic Considerations in Subacute and Chronic Hepatitis Med Clin No America 1947 *31* 1059

KARSNER H T *Morphology and Pathogenesis* of Hepatic Cirrhosis Am J Clin Path 1943 *13* 569

KATZIN H M WALLER J V and BLUMGART H L Cardiac Cirrhosis of the Liver A Clinical and Pathologic Study Arch Int Med 1939 *64* 457

KARUP N B and ROHOLM K The Development of Cirrhosis of the Liver After Acute Hepatitis Elucidated by Aspiration Biopsy Acta Med Scandinav 1941 *108* 306

LINTON R R JONES C M and VOLWILER W Portal Hypertension The Treatment of Splenectomy and Splenorenal Anastomosis with Preservation of the Kidney Surg Clin N America 1947 *27* 1162

MACMAHON H F and THANNHAUSER S J Xanthomatous Biliary Cirrhosis (A Clinical Syndrome) Ann Int Med 1949 *30* 121

MALLORY F B Cirrhosis of the Liver New England J Med 1932 *206* 1231

PATEK A J JR and others Dietary Treatment of Cirrhosis of the Liver Results in One Hundred and Twenty Four Patients Observed during a Ten Year Period J A M A 1948 *138* 543

THOMPSON R B Thrombosis of the Hepatic Veins The Budd Chiari Syndrome Arch Int Med 1947 *80* 602

VOLWILER W An Evaluation of Various Therapeutic Programs in Patients with Acute Fatty Livers Trans Assoc Am Physicians 1947 *60* 232

*Tumors of the Liver*

EWING J *Neoplastic Diseases 4th Ed* *Philadelphia* W B Saunders Company 1940 page 738

WILBUR D L WOOD D A and WILLETT F M Primary Carcinoma of the Liver Ann Int Med 1944 *20* 453

*Diseases of the Gall Bladder and Bile Ducts*

BOYDEN E A Effect of Natural Foods on Distention of the Gall Bladder with a Note on Change in Pattern of Mucosa as it Passes from Distention to Collapse Anat Rec 1925 *30* 333

GRAHAM E A and COLE W H Roentgenological Examination of *Gall Bladder Preliminary* Report of a New Method Utilizing Intravenous Injection of Tetrabromphenolphthalein J A M A 1924 *82* 613

GRAHAM E A and MACKEY W A Consideration of Stoneless Gallbladder J A M A 1934 *103* 1497

IVY A C and SANDBLOM P Biliary Dyskinesia Ann Int Med 1934 *8* 115

JONES C M Rational Use of Duodenal Drainage An Attempt to Establish a Conservative Estimate of the Value of this Procedure in Diagnosis of Biliary Tract Pathology Arch Int Med 1924 *34* 60

LAYNE J A and BERGH G S *Experimental* Study of Pain in Human Biliary Tract Induced by Spasm of Sphincter of Oddi Surg Gyn & Obst 1940 *70* 18

LYON B B V Diagnosis and Treatment of Disease of Gall Bladder and Biliary Ducts J A M A 1919 *73* 980

*Tumors*

Berk J E in Bockus H L Gastro-Enterology Philadelphia W B Saunders Company, 1944 *2* 711 788

Erdmann J F and Morris J H Polyposis of the Colon A Survey of the Subject Sur Gyn Obst 1925 *40* 460

Mayo C W Malignant Lesions of the Right Portion of the Colon Proc Staff Meet Mayo Clinic 1941 *16* 67

Ochsner A and Mahorner H in Pack G T and Livingston E M Treatment of Cancer and Allied Diseases New York Paul B Hoeber Inc 1940

Raiford T S Carcinoid Tumors of the Gastro-intestinal Tract (So-Called Argentaffin Tumors) Am J Cancer 1933 *18* 803

Rankin F W Bargen J A and Buie L A The Colon Rectum and Anus Philadelphia W B Saunders Company 1932

Rankin F W and Johnston C C Cancer of the Colon Chapter XL in Portis S A Diseases of the Digestive System Philadelphia Lea & Febiger 1941

*Ulcerative Colitis*

Bargen J A The Modern Management of Colitis Springfield Illinois Charles C Thomas 1944

Bockus H L Gastro-Enterology Philadelphia W B Saunders Company 1944 *Vol 2* Chapter LXII

Cattell R B The Surgical Treatment of Ulcerative Colitis Gastroenterology 1948 *10* 63

Daniels G L Psychiatric Factors in Ulcerative Colitis Gastroenterology 1948 *10* 59

Ginsberg R S and Ivy A C The Etiology of Ulcerative Colitis An Analytical Review of the Literature Gastroenterology 1946 *7* 67

Lindemann E Modifications in the Course of Ulcerative Colitis in Relationship to Changes in Life Situations and Reaction Patterns Life Stress and Bodily Disease Proceedings of the Association for Research in Nervous and Mental Diseases Williams & Wilkins 1950 *29* 706

McKittrick L S Moore F D and Warren R Ulcerative Colitis Ileostomy Problem or Solution? J A M A 1949 *139* 201

*Diseases of the Liver*

*Liver Physiology*

Best C H and Taylor N B The Physiological Basis for Medical Practice Baltimore The Williams & Wilkins Company 1950

Rich A R The Pathogenesis of the Forms of Jaundice Bull Johns Hopkins Hosp 1930 *47* 338

*Tests of Hepatic Function*

Ducci H and Watson C J The Quantitative Determination of the Serum Bilirubin with Special Reference to the Prompt Reacting and the Chloroform-Soluble Types J Lab & Clin Med 1945 *30* 293

Hawkinson V Watson C J and Turner R H Modification of Harrison's Test for Bilirubin in the Urine J A M A 1945 *129* 514

Iversen, P and Roholm K An Aspiration Biopsy of the Liver with Remarks on its Diagnostic Significance Acta Med Scandinav 1939 *102* 1

Kunkel H G Ahrens E H Jr and Eisenmenger W J Application of Turbimetric Methods for Estimation of Gamma Globulin and Total Lipid to Study of Patients with Liver Disease Gastroenterology 1948 *11* 499

Maclagan N F The Thymol Turbidity Test as an Indicator of Liver Dysfunction Brit J Exper Path 1944 *25* 234

Mateer J G Baltz J I Marion D F and MacMillan J M Liver Function Tests J A M A 1943 *121* 723

Watson C J Schwartz S Sborov S and Bertie E Studies of Urobilinogen V A Simple Method for the Quantitative Recording of the Ehrlich Reaction as Carried Out With Urine and Feces Am J Clin Path 1944 *14* 605

*Toxic Hepatitis*

Findlay G M and MacCallum F O Hepatitis and Jaundice Associated with Immunization against Certain Virus Diseases Proc Roy Soc Med 1938 *31* 779

Hanger F M and Gutman A B Post Arsphenamine Jaundice Apparently Due to Obstruction of Intra Hepatic Biliary Tract J A M A 1940 *115* 263

Ottenberg R and Spiegel R Present Status of Non obstructive Jaundice Due to Infections and Chemical Agents Causative Agents Pathogenesis Inter Relationships Clinical Characteristics Medicine 1943 *22* 27

Weir J F and Comfort M W Toxic Cirrhosis Caused by Cinchophen Arch Int Med 1933 *52* 685

Wilson J D and Goodpasture E W Yellow Atrophy of the Liver Acute Subacute and Healed Arch Int Med 1927 *40* 377

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Havens W P Jr Infectious Hepatitis Medicine 1948 *27* 279

Jones C M and Minot G R Infectious (Catarrhal) Jaundice An Attempt to Establish a Clinical Entity Boston Med and Surg J 1923 *189* 531

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Mallory T B The Pathology of Epidemic Hepatitis J A M A 1947 *134* 655

NEEFE J R STOKES J JR REINHOLD J G and LUKENS F D W Hepatitis Due to the Injection of Homologous Blood Products in Human Volunteers J Clin Investigation 1944 *23* 836

NEEFE J R Recent Advances in the Knowledge of Virus Hepatitis M Clin North America 1946 *30* 1407

ROHOLM K and IVERSEN P Changes in the Liver in Acute Epidemic Hepatitis (Catarrhal Jaundice) Based on 38 Aspiration Biopsies Acta Path and Microbiol Scandinav 1939 *16* 427

STOKES J JR and NEEFE J R The Prevention and Attentuation of Infectious Hepatitis by Gamma Globulin J A M A 1945 *127* 144

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CHALMERS T C and DAVIDSON C S A Survey of Recent Therapeutic Measures in Cirrhosis of the Liver New England J Med 1949 *240* 449

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GIBSON W R and ROBERTSON H E So-Called Biliary Cirrhosis Arch Path 1939 *28* 37

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GYORGY P Experimental Hepatic Injury Am J Clin Path 1944 *14* 67

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KATZIN H M WALLER J V and BLUMGART H L Cardiac Cirrhosis of the Liver A Clinical and Pathologic Study Arch Int Med 1939 *64* 457

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MACMAHON H E and THANNHAUSER S J Xanthomatous Biliary Cirrhosis (A Clinical Syndrome) Ann Int Med 1949 *30* 121

MALLORY F B Cirrhosis of the Liver New England J Med 1932 *206* 1231

PATEK A J JR and others Dietary Treatment of Cirrhosis of the Liver Results in One Hundred and Twenty Four Patients Observed during a Ten Year Period J A M A 1948 *138* 543

THOMPSON R B Thrombosis of the Hepatic Veins The Budd Chiari Syndrome Arch Int Med 1947 *80* 602

VOLWILER W An Evaluation of Various Therapeutic Programs in Patients with Acute Fatty Livers Trans Assoc Am Physicians 1947 *60* 232

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IVY A C and SANDBLOM P Biliary Dyskinesia Ann Int Med 1934 *8* 115

JONES C M Rational Use of Duodenal Drainage An Attempt to Establish a Conservative Estimate of the Value of this Procedure in Diagnosis of Biliary Tract Pathology Arch Int Med 1924 *34* 60

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LYON B B V Diagnosis and Treatment of Disease of Gall Bladder and Biliary Ducts J A M A 1919 *73* 980

*Tumors*

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Mayo C W Malignant Lesions of the Right Portion of the Colon Proc Staff Meet Mayo Clinic 1941 *16* 67

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Bockus H L Gastro-Enterology Philadelphia *W B Saunders Company 1944 Vol 2 Chapter* LXII

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Daniels G E Psychiatric Factors in Ulcerative Colitis Gastroenterology 1948 *10* 59

Ginsberg R S and Ivy A C The Etiology of Ulcerative Colitis An Analytical Review of the Literature Gastroenterology 1946 *7* 67

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Hawkinson V, Watson C J and Turner R H Modification of Harrison's Test for Bilirubin in the Urine J A M A, 1945 *129* 514

Iversen P and Roholm K *An Aspiration* Biopsy of the Liver with Remarks on its Diagnostic Significance Acta Med Scandinav 1939 *102* 1

Kunkel H G Ahrens L H Jr and Eisenmenger W J Application of Turbimetric *Methods for Estimation of Gamma Globulin* and Total Lipid to Study of Patients with Liver Disease Gastroenterology 1948 *11* 499

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Ottenberg R and Spiegel R Present Status of Non-obstructive Jaundice Due to Infections and Chemical Agents Causative Agents Pathogenesis Inter Relationships Clinical Characteristics Medicine 1943 *22 27*

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Wilson J D and Goodpasture E W Yellow Atrophy of the Liver Acute Subacute and Healed Arch Int Med 1927 *40* 377

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Havens W P Jr Infectious Hepatitis Medicine 1948 *27* 279

Jones C M and Minot G R Infectious (Catarrhal) Jaundice An Attempt to Establish a Clinical Entity Boston Med and Surg J *1923 189 531*

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Mallory T B The Pathology of Epidemic *Hepatitis J A M A 1947 134* 655

# Chapter 28

# Diseases of the Locomotor System

By STACY R. METTIER, M.D.

## THE JOINTS

### Arthritis

The amount of morbidity and invalidism produced by diseases of the locomotor system is appalling. It has been estimated that *320,000 persons are rendered unemployable annually* by the rheumatic diseases alone.

In recent years an increasing amount of interest has been shown in the subject of arthritis by physicians and investigators alike. In the Scandinavian countries hospitals have been set aside solely for the care of patients with diseases of the joints.

Some idea of the tremendous amount of interest shown in this subject may be gained from the fact that the material from the Eighth Rheumatism Review which appeared in *1940* was culled from *616* articles and *8* books. During World War II, the review was discontinued but it reappeared again in 1948 with information abstracted from 1995 articles.

The American Rheumatism Association adopted the following provisional classification at its June 1941 meeting:

1. Specific infectious arthritis (organism known)
   - (*a*) Gonorrheal arthritis
   - (*b*) Pneumococcal arthritis
   - (*c*) Tuberculous arthritis
   - (*d*) Brucellosis arthritis
2. Arthritis of rheumatic fever
3. Rheumatoid arthritis (synonyms: atrophic, proliferative and chronic nonspecific infectious arthritis, Still's disease, Marie-Strumpell spondylitis)
4. Osteo-arthritis (synonyms: degenerative joint disease, hypertrophic senescent arthritis)
5. Arthritis of immediate traumatic origin
6. Arthritis of gout
7. Arthritis of neuropathic origin (Charcot's joint)
8. Neoplasms of joints
9. Miscellaneous forms (arthritis associated with other diseases)

The term "rheumatism" has come down to us through the ages. It is a poor term but according to Snyder it still remains the best word to use in referring to that large group of diseases characterized by pain and stiffness in the ligaments, muscles and joints.

*Examination of the Patient.*—In attempting to make a diagnosis it is advisable to follow a well formed plan of study. A carefully taken medical history should include an inquiry into possible familial predisposition to disease of the joints or muscles, past history of rheumatic fever and exposure to or infection with gonococcus, tubercle bacillus, pneumococcus or other infectious agents that tend to be of a recurrent nature and are

McCall M and Tuggle A Calcium Bile Clinical and Pathological Study Am J M Sc 1942 *203* 413

Rous P Drury D R and McMaster P D Some Causes of Gall Stone Formation, on Certain Nuclei of Deposition in Experimental *Cholelithiasis* J *Exper Med* 1924 *37* 97

Stewart H L Lieber M M and Morgan D R Carcinoma of the Extrahepatic Bile Ducts Arch Surg 1940 *41* 662

Walsh E I and Ivy A C Observations on Etiology of Gall tones Ann Int Med 1930 *4* 134

Walters W and Snell A M Diseases of the Gallbladder and Bile Ducts Philadelphia W B Saunders Company 1940

*Diseases of the Pancreas*

Archibald I H Diseases of the Pancreas in Nelson s Loose-leaf Surgery New York Thomas Nelson & Sons 1934 1 *ol* 5

——— The Experimental I roduction of Pancreatitis as a Result of Resistance of the Common Duct Sphincter Surg Gyn & Obst 1919 *28* 529

Best C H and Taylor N B The Physiologic Basis of Medical Practice Baltimore The Williams & Wilkins Company 1950 page 529

Dragstedt L R Hammond H E and Ellis S C *Pathogenesis of Acute Pancreatitis* (Acute Pancreatic Necrosis) Arch Surg 1934 *28* 232

Fitz R Acute Pancreatitis Boston Med & Surg J 1889 *120* 181

Rich A R and Duff G I Experimental and Pathological Studies on the Pathogenesis of Acute Hemorrhagic Pancreatitis Bull Johns Hopkins Hosp 1936 *58* 212

Whipple A O Observations on Radical Surgery for Lesions of the Pancreas Surg Gyn & Obst 1946 *82* 623

Wirts C W Jr and Snape W J Disseminated Calcification of Pancreas Subacute and Chronic Pancreatitis Am J Med Sc 1947 *213* 290

may be the association of keratotic areas in the skin with polyarthritis This combination is being given consideration as a distinct entity and is described in the literature as 'keratosis blenorrhagica Ninety seven cases have been collated from the literature It is noted that the joint manifestations usually precede the appearance of the skin lesions The condition is unusual in that there is simultaneous involvement of several joints which in addition to the usual site may include the acromioclavicular joints

*Treatment of Gonorrheal Arthritis and Gonorrheal Rheumatism* —*See* Chapter 5

### Tuberculous Arthritis

Recent reviews indicate that tuberculous arthritis is of less frequent occurrence than formerly reported This decline is attributed to strict supervision over tuberculin tested milk cows, and to better eating and good hygienic habits on the part of the people

Tuberculous arthritis usually is monarticular in distribution In Dickson's report of 158 cases of tuberculous arthritis the frequency with which the joints were involved was as follows the spine in 62 cases hip in 41 knee in 25 ankle in 11 wrist in 10 sacro-iliac in 6 shoulder in 2 and elbow in 1 case The symptoms of tuberculous arthritis are generally characterized by the slow insidious development of pain and swelling There may be slight local warmth If a weight bearing joint is involved the patient may limp As the disease progresses pain and stiffness increase especially if the synovia is involved Affected children not infrequently utter night cries and may exhibit jerking of the lower extremities due to relaxation of the spastic muscles The disease at first may be extra articular and exist for years before rupturing into a joint cavity

*Tuberculosis of the Spine* (*Pott's Disease—Tuberculous Spondylitis*) is a local manifestation of a chronic tuberculous infection elsewhere in the body Trauma may be a predisposing factor in the development of a locus minoris resistentiæ The process begins most often in the cancellous portion of the anterior part of the body of the vertebra



One or more of the lower thoracic vertebræ may be damaged, and as the disease progresses bone is destroyed and finally the structure of the vertebra collapses Caseation of tissue leads to abscess formation Such an abscess may undermine the anterior common ligament and spread by extension to the adjacent vertebræ or extend along the anterior surface of the spine to form a psoas abscess

### Brucellosis

### (*Undulant Fever, Malta Fever*)

Acute polyarthritis may occur during the course of brucellosis In the acute phase of illness, arthralgia generalized body aches muscle pains and backache may be severe Joint manifestations usually are transitory and persistence of chronic joint disease seldom occurs Intermittent hydrarthrosis may develop but does not lead to suppurative arthritis

### Arthritis in Other Infectious Diseases

Of the numerous cases reported of arthritis as a complication of *lobar pneumonia* the incidence varies from as low as 0 1 to 6 5 per cent Since the introduction of chemotherapy it has almost disappeared The arthritis is usually monarticular and shows effusion in the joint cavity and swelling of the periarticular tissues Cultures should be made of fluid aspirated from the joint in order to be certain of the infectious agent

Articular swelling may appear during the course of *typhoid fever* It may be monarticular or polyarticular in distribution Usually the swelling is due to a serous effusion which may become septic Spondylitis (typhoid spine) may arise as a complication of typhoid fever

An arthrosis may be seen occasionally in subacute bacterial endocarditis The joints are usually painful slightly reddened and show only slight or a moderate degree of swelling The swelling is transitory

Arthritis is not an uncommon finding in *cerebrospinal meningitis* It may be monarticular or polyarticular The synovial

focal in distribution The environment of the patient should be determined with regard to exposure to extremes of temperature and humidity as well as to prolonged hours of work undue fatigue or severe mental shock It is important to know about repeated trauma of one kind or another to the joints The dietary habits of the patient can best be determined by a well trained dietitian However, since there is evidence to show a relationship between dietary deficiencies and diseases of the musculoskeletal system, physicians may obtain some information relative to deficiencies after careful analysis of the patient s eating habits absorption and utilization of food etc See Chapter 14

The development of the history of the present illness should include such details as the date of onset of muscular atrophy or paralysis, bone tenderness and pain in or about a joint The description of the joints should mention the degree of swelling tendency to disappear and recur, and distribution Most patients with chronic illness especially joint disease, have tried various remedies before consulting the physician It is advisable therefore to include these in the history

A detailed physical examination must be made The posture, gait, habitus and general attitude of the patient should be recorded Examine the ears for tophi the skin for subcutaneous nodules and the various joints for tender or swollen bursae Search for foci of infection Determine whether the patient has a tendency to bruise easily and look for minute hemorrhages in the skin and beneath the finger nails Atrophy of the muscles and power of contraction should be noted The color and temperature of the skin about a joint the degree of moisture of the palms of the hands and feet the tenderness of the bones and muscles may give details of information that may be of value in differential diagnosis

In making the diagnosis of musculoskeletal disease, one must when possible include certain laboratory procedures When anemia is encountered an accurate estimation of the hemoglobin and enumeration of the red blood cells is indicated The total white blood cell count and the filament and non filament differentiation aid in determining the degree of activity of a given process Estimation of the rate of sedimentation of the erythrocytes becomes a valuable laboratory aid in the study of patients with rheumatoid arthritis A determination of the blood uric acid, the Wassermann reaction and the gonococcus fixation test are of help in differentiating puzzling cases of swelling of the joints In recent years a technic has been devised for the growth of gonococci on special media Roentgen ray examination of at least one of the involved joints or bones should be made Removal of synovial fluid for culture and cell count, and biopsy of synovial membrane muscle or bone are other procedures which may prove of aid when wisely chosen

SPECIFIC INFECTIOUS ARTHRITIS
*(Organism Known)*

GONORRHEAL ARTHRITIS OR GONORRHEAL RHEUMATISM —In the past it has been estimated that as many as 5 per cent of the persons infected with the gonococcus develop gonorrheal arthritis The initial infection need not be the usual genital one It may be proctitis or extragenital or even an ophthalmia Since the introduction of new drugs (sulphonamide and its derivatives and penicillin) and fever therapy in the treatment of this disorder the incidence of the articular complications has fallen to less than 0 5 per cent

Rheumatism associated with gonococcal infection may show considerable difference between the time of infection and the onset of symptoms and display considerable variation in its manifestations For consideration of gonorrheal arthritis see Chapter 5

CHRONIC GONORRHEAL RHEUMATISM

This condition may closely simulate rheumatoid arthritis There is a polyarthritis involving the interphalangeal carpal and carpo metacarpal joints as well as the joints of the knees and feet Pain and tenderness of the volar surface of the calcanei frequently are present There is a tendency to fibrosis contracture and ankylosis as is found in rheumatoid arthritis

An unusual feature of gonorrheal arthritis

Predisposing causes are exposure fatigue and exhaustion or physical and emotional shock such as grief and worry The onset may follow any exhausting disease

Foci of infection have long been held as etiologic factors in rheumatoid arthritis The tonsils sinuses middle ear gall bladder and prostate have been reported to be the sites of infection Contrary to expectations there was found to be no lessening of the arthritis following their eradication An objection to the theory pertaining to focal infection in arthritis could be made on the ground that such focal infection sometimes is found upon close study in persons who show no signs of arthritis Mention should be made that arthritis may be seen to develop rapidly in cases of infection with retention of pus The writer recalls an incidence wherein a physician was suffering from infection about the root of a tooth His ankles and knees suddenly became swollen red and painful Adequate drainage of the tooth socket was established serosanguineous pus exuded and the joint swelling disappeared spectacularly This is clearly an example of infectious arthritis

Whether or not rheumatoid arthritis is a manifestation of tissue sensitivity or allergy to some bacterial infection or to food is still a matter for further investigation This hypothesis would presuppose that an allergen absorbed into the blood-stream from some focus of infection or from the intestinal contents would have the power to sensitize synovial tissue Perhaps the presence of allergy in a susceptible individual may play a role in acute joint swelling but it is difficult to apply this to a state of chronic swelling

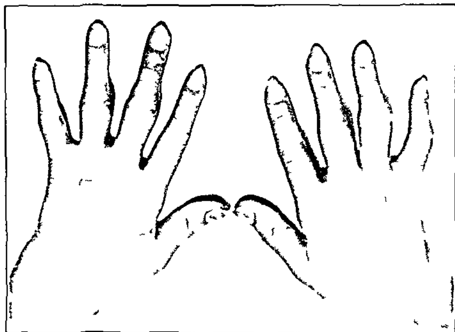


FIG 215 —Rheumatoid arthritis showing swelling of the metacarpophalangeal joints Note fusiform swelling of proximal interphalangeal joints

There is evidence to show that an abnormality of the nervous system is present in rheumatoid arthritis Almost invariably there is marked sweating of the hands and feet This is not to be accepted as the usual suderesis and the cooling off process associated with a febrile condition but rather as a localized sign of instability of the vasomotor system Blanching of the fingers is another example of involvement of the nervous system This phenomenon with its appearance suggestive of Raynaud s disease is frequently seen and found to precede the development of arthritis The atrophy of muscles the thin waxy appearance of the

fluid usually is serous in quality and may become purulent

A transitory phase of joint swelling occasionally accompanies such infections as Haverhill fever puerperal fever influenza, scarlet fever, mumps chronic ulcerative colitis and erysipelas The joint manifestations are largely symptomatic and in almost all instances there is a complete return of joint function

Should the effusion become septic surgical drainage may be indicated

ARTHRITIS OF RHEUMATIC FEVER

*Rheumatic Fever* —Since joint pain and swelling are well known to be a part of the symptomatology of rheumatic fever they will be given brief consideration here

The larger joints are usually affected first the knees ankles shoulders and wrists apparently being the more vulnerable ones However there may be involvement of the elbow joints and hips, and the smaller joints of the feet and hands There may be a monarticular or polyarticular distribution throughout the body A striking feature of rheumatic arthritis is its tendency to shift from one joint to another Wherein one articulation may be affected suddenly all signs of inflammation will subside to reappear in one or more other joints

Pain is the outstanding symptom The joints are tender to the touch and slight pressure is sufficient to make the patient wince or cry out The overlying skin usually is slightly reddened but not invariably so There may be slight or considerable evidence of synovial swelling, and accordingly the tumefaction may be soft firm or fluctuant, depending upon the degree of tension

The histologic examination may reveal the joint cavity to be the site of an acute inflammatory process Klinge described the changes in detail, he stated that there is a hyperplasia of the synovial epithelium within and upon which are streaks of fibrinoid necrosis, the connective tissue appears edematous and is infiltrated with leukocytes a hyaline fibrinous material is to be seen free in the joint space

There is some experimental evidence to show that these pathologic changes are strikingly similar to those found in the joints of scorbutic guinea pigs Rinehart and Mettier produced chronic scurvy in guinea pigs and subjected them to superimposed infection (beta streptococcus) An arthropathy appeared which was considered to be fundamentally similar in character and distribution to that of rheumatic fever Of considerable interest in this connection is a statement by T Duckett Jones who observed that epistaxis and splinter hemorrhages beneath the finger nails are a frequent accompaniment of rheumatic fever Large doses of vitamin C administered to patients with rheumatic fever have acted to prevent this phenomenon and caused the hemorrhagic tendency to disappear

RHEUMATOID ARTHRITIS

*Synonyms* — Atrophic Non suppurative arthritis deformans Chronic infectious arthritis Proliferative arthritis

*Definition* —A disease of the joints of unknown etiology characterized by an inflammatory reaction in the synovial membrane and periarticular structures effusion in the joint cavity and atrophy of the regional bony and muscular structures Early in the course of illness there is pain and stiffness due to swelling and muscle spasm Later there is deformity and loss of joint function due to ankylosis The disease tends toward chronicity and a polyarticular symmetrical distribution

*Incidence* —At present there are no accurate figures concerning the incidence of rheumatoid arthritis

Rheumatoid arthritis is found more frequently in women than in men It occurs with great frequency in the temperate zones the geographic distribution of this disease is the same as that of rheumatic fever It is world-wide in distribution but is infrequent in the tropical and sub tropical climates

*Etiology and Pathogenesis* —The cause of rheumatoid arthritis is unknown Whereas some investigators consider it to be infectious in origin others regard it as due to a deficiency in certain vitamins the result of altered metabolism or possibly to an abnormality in endocrine function

brilliantly eosinophilic hyalinized fibrin

*Symptoms and Course of Illness*—The onset of illness may show extreme variations Individual susceptibility and resistance to the disease are evident Very little emphasis has been placed on the insidiousness with which rheumatoid arthritis may develop Occasionally patients are seen who complain of weakness lassitude and rather vague and fleeting joint pain There may be few or no signs of inflammation After some weeks or months stiffness and slight swelling make their appearance in a number of the small joints especially the carpal joints *These signs tend to disappear and recur repeatedly* Eventually the changes become increasingly severe and finally are persistent

In other patients the beginning may resemble an attack of acute rheumatic fever Extreme prostration a high fever at the onset rapid pulse moderate leukocytosis enlargement of the spleen and generalized adenopathy all denote an infectious process As the disease progresses it becomes distinguishable from rheumatic fever by its symmetry in distribution and the periarticular changes which are more in evidence and more permanent in nature

The smaller joints of the extremities the wrists and ankles are usually the first to become involved swelling on the dorsal surface of the metacarpal bones stiffness and weakened grip of the hand may be noted Involvement of the interphalangeal joints shows a quite characterisic picture There is a fusiform swelling of the middle joints due to an excess of synovial fluid periarticular edema and infiltration The patient finds it difficult or impossible to close his hand The metacarpophalangeal joints and the metatarsophalangeal joints may also become involved in the process Eventually the elbows shoulders knees spine the sacro iliac and acromioclavicular joints and not infrequently the articulation of the jaw show evidence of the disease

In the acutely involved joints there is redness heat extreme tenderness and pain Over a period of time the redness and pain may subside but the heat and tenderness persist In the gradually advancing cases the findings are less pronounced the joints may seldom show redness but the tenderness may be acute and of diagnostic significance

The course of illness in some instances is subacute After a period of weeks or a few months some of the joints clear up and are restored to usefulness A tendency toward spontaneous remission exists and although every joint in the body may have been crippled at one time the signs of an acute inflammatory process subside Under these circumstances the function of some joints will return but others will suffer permanent loss of function as a result of the inflammatory sequels

The chronic form of illness is most frequently *encountered by the physician* Following the inflammatory phase in the joints, or coinciding with it the characteristic atrophy of muscles appears In a few instances the atrophy may precede the *joint swelling Loss of function* occurs in muscle groups about an involved joint and is usually symmetrical

As time goes on contracture of unapposed muscles makes an appearance fibrosis ankylosis and destruction of cartilage progresses in the joints and varying degrees of disability appear In the hands the fingers assume an ulnar deviation The stresses of contracture and the loss of cartilage produce sharp flexion of some of the terminal phalanges The disability may be accentuated by subluxation of the middle phalanges Power to flex and extend the hand at the wrist is lost early because of fusion of the metacarpal bones Movements requiring coordination of muscle such as supination of the hand flexion and extension of the forearm elevation and rotation of the humerus are lost and contribute to the disability of the patient In the lower extremities similar structural changes occur, and when marked in the toes ankles and knees the patient becomes bedridden and helpless

In the *slowly advancing cases of rheumatoid* arthritis loss of weight is apparent and the patient becomes rapidly emaciated The atrophy of muscles loss of subcutaneous fat and thinning of skin over the *joints all accentuate the swelling of periarticular* and joint structures Loss of appetite flatulence constipation low blood pressure weakness and hypochromic anemia contribute to the patient s general debility

skin, the brittleness of the finger and toe nails, and thinness of the cortex of bones may be other indications of trophic changes wrought through influences of the nervous system.

Some mention should be made of the altered psyche in patients with rheumatoid arthritis. Mental depression, loss of interest in environment, utter hopelessness with regard to the future, and abandonment of the will to help oneself are attitudes seen in arthritic patients.

In summing up the available data on the etiology of rheumatoid arthritis it appears that the disease usually manifests the characteristics of an infectious process. Fever, leukocytosis, rapid sedimentation rate, and signs of inflammation in the synovia suggest this possibility. The finding of agglutinins and precipitins for streptococcus in the blood in a high percentage of patients offers strong evidence for this bacterium as the source of the disease. The sequence of events resulting in structural changes possibly depends upon local sensitization of joint structures, low plasma ascorbic acid, and influences resulting from damage of the organic or functional nervous system.

The possibility that some biochemical disturbance resulting from endocrine dysfunction might be at fault in the pathogenesis of rheumatoid arthritis becomes likely in view of the recent publications of Hench and his associates on the favorable effect of Compound E (Cortisone acetate) on the rheumatic state.

*Pathology*.—In recent years much has been added to the knowledge of the synovial fluid and the synovial membrane in health and in disease. The works of Allison and Ghormley, Coombs, Kling and Bauer and his associates are among the more important contributions on this subject, and in them is to be found a more adequate concept of the structural changes of the synovial membrane in rheumatoid arthritis.

The synovial sac is distended and increased in size due to effusion of synovial fluid. The quantity that may be aspirated from a knee joint may vary from as little as 15 cc. to as much as 150 cc. It appears more or less turbid. Cell counts done on the fluid from a large series of cases were found to average from 10,000 to 20,000 cells per cu. mm. The percentage of polymorphonuclear leukocytes is high in the majority of cases. The fluid usually gives an alkaline reaction to litmus and shows a positive reaction for mucin.

The most constant finding in the synovial membrane in rheumatoid arthritis is a proliferative reaction. The synovial villi are thickened, there is a lymphocytic infiltration of the tissues, and there is some evidence of fibroblastic hyperplasia. A fibrinous material intermingles with tongue-like outgrowths resulting from proliferative reaction and extending into the joint cavity and over the articular surfaces to form a pannus. The organization of this fibroid material leads to the development of ankylosis.

The periarticular tissues are also involved in the process. Analogous changes are present in the connective tissue beneath the synovial membrane and in the tendons inserting around the joint. Edema, infiltration with lymphocytes, increased numbers of connective tissue cells and hyaline streaks of fibrin all add to the swelling, deformity and limitation of movement of the joint.

Retrogressive changes are apparent in the articular cartilage. Areas of destruction and necrosis may be seen. Attempts at repair are recognized elsewhere by undifferentiated and at times vascularized connective tissue. There is a general thinning of the cartilage and subjacent bony trabeculæ. As the cartilage undergoes absorption and fibrous replacement, calcification or ossification of this fibrous tissue takes place. The center of the end portion of the bone shows absorption in irregular areas. The new bone formation is more active toward the periphery.

Interesting subcutaneous nodules are found in a high percentage of patients. They usually are felt beneath the skin about the joints, but occasionally are encountered attached to an underlying bony structure. These nodules show the histologic characteristics of the rheumatic granulomas. On microscopic examination the tissue seems to be edematous and made up largely of a cellular fibrous tissue in the interstices of which may be seen irregular strands of

kyphosis The arms hang loosely from the rigid spine and the patient acquires a waddling gait

The most valuable aid in the diagnosis of rheumatoid arthritis of the spine is the appearance of the changes in the roentgenographic film In the sacroiliac joints the changes may vary from narrowing of the joint which is an early sign, to irregular proliferation of the margin and osteoporosis of the adjacent bone and signs of complete ankylosis The most important joints to be examined are the apophyseal joints Until recently they have been given little attention (Fig 217) Special oblique views are necessary to demonstrate any changes Here again the early finding may be that of narrowing or clouding of the joint spaces In far advanced cases the common finding is that of calcification of the anterior and lateral ligaments

The treatment of rheumatoid arthritis of the spine requires the combined efforts of physician orthopedist roentgenologist and physiotherapist At present the most valuable means of preventing the advance of the disease is *x* ray directed down the entire length of the spine The technique generally used in our clinic is as follows In people of average length four portals are placed longitudinally along the vertebral column a single field placed horizontally to cover the sacroiliac joints The most superior field measures 10 by 10 centimeters and the others 10 by 15 centimeters In shorter people the spine is easily covered by three 10 by-15 centimeter portals placed longitudinally the sacro iliac port is transversely situated as before The fields are delineated with indelible skin marking ink so that the treatment cone may be placed identically each time This inked boundary of adjacent portals results in separation of the fields by from 5 to 7 millimeters



Fig 217 —Marie-Strumpell spondylitis of cervical vertebræ

Under these circumstances the sedimentation rate is increased, there is slight leukocytosis and a moderate elevation of temperature

Patients may suffer from little pain while exhibiting advanced stages of the disease When the signs of inflammation have subsided the periarticular skin may continue to show *an elevation of temperature* In the presence of cold damp weather there is apt to be a return of pain and temporarily increased stiffness especially at night seen in some joints, and fibrosis, loss of cartilage and ankylosis are seen in others

RHEUMATOID SPONDYLITIS SPONDYLITIS *DEFORMANS* (*SPONDYLOSE RHIZOMELIQUE*, MARIE-STRUMPELL DISEASE) —Spondylitis deformans is a manifestation of rheumatoid arthritis in the vertebral column and its ligamentary attachments It may be confined to the spinal column or appear as part of a generalized rheumatoid arthritis

Early in the disease there is limitation of motion of the lumbar or cervical spinal segments due to pain and muscle spasm The disease progresses and finally all of the verbebræ are involved There is fixation of *the spinal column which may* be almost complete due to ossification of the ligaments and bony ankylosis The ribs become fixed the chest flattened and the entire spine may be totally rigid *There is frequent* involvement of the hips and shoulders (rhizomelique) although these joints often escape

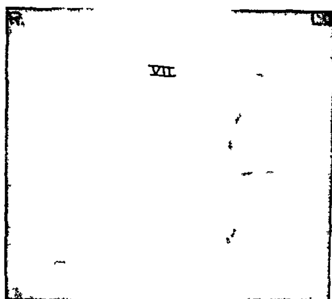



FIG 216 —Rheumatoid Spondylitis

The *roentgen ray examination* of the patient may reveal no abnormalities in the joints in the early stages Fusiform effusion in the interphalangeal joints giving rise to *soft tissue swellings may be noted* before any change in the density of bony structure is discovered Among the early changes is rarefaction of the trabeculated ends of the bone The *zone of calcification* however is preserved The joint space will be widened along with the effusion Later the joint space is narrowed and atrophy of the bone ends is evident *Finally there is* generalized decalcification, but reparative calcareous lipping will persist Enlarged punched out areas of bone atrophy appear, these are commonly encountered in *rheumatoid* arthritis as well as in gouty arthritis Deformity due to softening and subluxation of bone may be

On examination in the early stages of the disease the spine may appear straight The presence of an abnormality may be detected only after careful examination for muscle spasm or the fixation of two or three vertebræ As ankylosis of the vertebræ progresses the spine bends and the stature of the patient shortens due to marked

acerbations and remissions rather than to a steady progression of symptoms The terminal phalangeal joints of the fingers and toes are more frequently involved and usually are symmetrical The nails of the fingers and toes show changes usually found in psoriasis Atrophy of the bone may be extreme in these cases of psoriatic arthritis

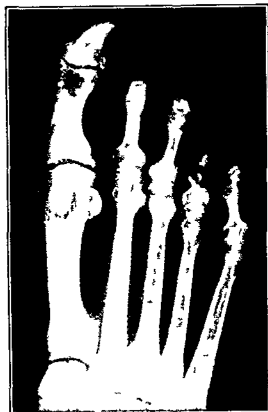


Fig 218 —Psoriatic arthritis There is a loss of bony substance of the terminal phalanges

Reiter's Disease —This disease is characterized by arthritis involving one or more joints and associated with urethritis conjunctivitis and keratinizing skin lesions A number of cases have now been reported and so far have been limited entirely to males The joint swelling may last for a period of weeks or months and tends to undergo relapse followed by remission So far no specific bacteriologic agent has been isolated

Palindromic Rheumatism —Palindromic rheumatism is thought by some to be a true syndrome but by others to be an unusual form of rheumatoid arthritis The clinical manifestations consist of repeated afebrile attacks of acute or subacute arthritis accompanied by pain swelling redness and disability A single joint is usually involved only rarely are there evidences of the inflammatory process in multiple joints The onset of illness is usually abrupt it lasts for a few days only completely disappears and then recurs at varying intervals It appears in adults of either sex There are no laboratory tests of diagnostic value

*Differential Diagnosis* —The differential diagnosis of rheumatoid arthritis is seldom difficult in patients with a slowly progressive form of the disease In patients with an acute fulminating arthropathy associated with fever leukocytosis and red swollen joints the resemblance to rheumatic fever is so close that differentiation is difficult Soon however the acute phase subsides and there appear the periarticular changes which characterize the chronic form of the disease

The differentiation from degenerative joint disease (osteo-arthritis) is set forth in table 63

It is important to emphasize the fact that rheumatoid arthritis and degenerative joint disease may occur in the same individual A person in the fifth or sixth decade with osteophyte formation of the knees may show a superimposed rheumatoid arthritis

Rheumatic fever relatively afebrile and running a subacute course may simulate rheumatoid arthritis This is especially true in ambulatory patients The distinction becomes clear when the patient develops signs of mitral valvulitis or periarthritis Valvulitis is not a feature of rheumatoid arthritis however we have observed several cases of mitral stenosis and insufficiency in patients with spondylitis deformans

Gonococcal arthritis may be readily mistaken for rheumatoid arthritis in women without evidence of vaginal discharge A history of exposure to possible infection may be denied The diagnosis will rest largely on the possibility of obtaining cultures of the gonococcus from the cervix the bloodstream or the joints involved A strongly positive gonococcus complement fixation test will aid in the diagnosis A history of shaking chill may be diagnostic of gonococcal bacteriemia whereas this phenomenon seldom occurs in rheumatoid arthritis

Using $x$-rays generated by 200 kilovolts constant potential H.V.L. 1.05 millimeters copper, 50 centimeters target-skin distance, and an output of approximately 45 roentgen a minute, 200 roentgen (air) are delivered to the upper and lower halves of the vertebral column and paraspinal musculature on alternate days for a total of 600 roentgen (air) per field.

For treatment of a chronic inflammatory lesion on the surface, it is desirable to deliver from 75 to 150 roentgen to the process at each treatment. For surface lesions, beams of "softer" quality are adequate, but in order to deliver the same dose at the depth with which we are concerned, it is felt that a beam of the quality described is more appropriate. The 200 roentgen (air) is equal to 263 skin roentgens on the 100 square centimeter field and 273 skin roentgenograms on the 150 square centimeter fields. At the average depth of 7 centimeters the calculated tissue dose, therefore, is 121 roentgen and 134 roentgen respectively.

After a rest period of four weeks, a second identical course of treatment is given, and after a second rest period of twelve weeks, the third and final course of treatment is administered.

From twenty-four to forty-eight hours after the first exposure, the patient will experience relief. The mode of action of the roentgen ray in relieving pain in rheumatoid arthritis is not understood, but it is felt that it causes a dissolution of the inflammatory process and has a tendency to lessen muscle spasm. Treatments are given daily for a period of one week, followed by a rest period of four weeks. Then a second course of treatment is given; this is followed by a rest period of three months before the third and final course of treatment is given.

Exercises to regain lost range of motion of the spine should be conducted under supervision of the physiotherapist. This may best be done after exposure to radiant heat followed by massage, passive exercises and then active exercises which will tend to cause forward flexion of the spine. The importance of a proper posture must be stressed and all patients instructed in exercises to maintain a normal stance and strengthen the back muscles. Deep breathing exercises should be resorted to three times daily in an endeavor to increase the movement of the thoracic cage.

This method of treating rheumatoid arthritis of the spine has been used in our clinic since 1941 with gratifying results. There have been very few failures, and in most of these there has been alleviation of symptoms after a second course of therapy.

## Miscellaneous Types of Rheumatoid Arthritis

**Juvenile Rheumatoid Arthritis (Still's Disease).**—In 1897 Still described cases of arthritis in children associated with splenomegaly, adenopathy and leukopenia. Since then other cases have been reported in the literature. The histologic changes in the lymph nodes and spleen have not been considered specific for any disease. The course of illness, the tendency toward bony ankylosis and muscle atrophy are comparable to those in adults.

**Rheumatoid Arthritis of Adults With Splenomegaly, Adenopathy, Anemia and Leukopenia (Felty's Syndrome).**—Felty in 1924 reported a group of five cases of chronic arthritis in patients with leukopenia and splenomegaly. Curtis and Pollard compared the clinical findings and histologic changes in cases of Felty's syndrome with those of rheumtaoid arthritis with splenomegaly and leukocytosis and another group with rheumatoid arthritis but without splenomegaly or leukopenia. They found that the pathologic reactions in the spleen, lymph nodes and bone marrow were nonspecific.

**Rheumatoid Arthritis With Psoriasis (Psoriatic Arthritis, Psoriasis Arthropathica).**—The occurrence of psoriasis with rheumatoid arthritis has been the subject of discussion in approximately 200 cases reported in the literature. Some authors maintain that psoriatic arthritis is a separate disease entirely; others believe the combination of skin and joint changes to be a matter of coincidence. There are certain clinical features, however, that differ from the usual ones found in rheumatoid arthritis. There is a tendency toward ex

active process in approximately 50 per cent of cases treated with chrysotherapy.

Before outlining my plan for the treatment of rheumatoid arthritis it may be well to discuss a failure which is directly due to the physician himself. Most articles dealing with the treatment of arthritis emphasize the need for rest. Taken literally, the patient is placed in bed and his wants cared for without so much as the elevation of his hands. After months of bed rest the feet become rotated outward from pressure of the bed clothes, the knees are fixed and the arms held rigidly to the sides of the body. Thus the patient becomes an abject figure and totally disabled as a result of the prolonged inactivity.

The treatment of rheumatoid arthritis should be carried out systematically and with careful attention to many details.

The activity of the process must be gauged and methods of treatment employed to meet the individual case; this applies to rest, muscular activity, diet, physical therapy and medication.

In general the patients may be divided into groups—those ambulatory and those requiring bed rest. In so far as possible and with due caution for their health we encourage patients to be ambulatory and busy. This helps to keep up their morale, maintain muscle tone and prevent ankylosis.

The patient requiring bed rest is usually emaciated and suffering from exquisite pain on motion of the joints. Fever, slight leukocytosis and moderate anemia may be present. Rest for this type of patient should be relaxing in so far as possible. The bed should be firm in order to avoid sagging. The weight of the blankets must be kept off the feet of the patient by draping them over a wooden frame support or pillows tucked in at the foot of the bed. Sand bags or partial casts may be employed to keep the extremities in good alignment and to reduce muscle spasm. One or more times daily each joint should be gently flexed and extended to break down fibrous growth and prevent ankylosis. The use of splints and casts for the purpose of immobilization is to be discouraged. The application of such apparatus promotes ankylosis and permanent disability of a joint.

Adequate nutrition must be maintained. Gain in weight in undernourished patients is usually a sign of improvement, whereas loss in weight offers a grave prognosis. A total intake of from 2000 to 3000 calories should be encouraged, depending upon the size of the patient. Milk, fruits, meats and fish are indicated. Pemberton believes there is increased absorption of carbohydrates from the intestinal tract in patients with rheumatoid arthritis and accordingly advocates the avoidance of too much starch. Rinehart has shown there is a decrease in the utilization of vitamin C in patients with this disease. An adequate supply of vitamin C may be insured by drinking 400 to 600 cc. of fresh orange juice daily. The orange juice may be supplemented by ascorbic acid preparations (i. e. cevitamic acid 0.050 three times daily). Added vitamin concentrates A, B and D may aid in regaining the general nutrition of the patients.

Effecting the relief of pain arising in the joints, especially during the acute phase, becomes a problem for the physician. There is reason to believe that the salicylates not only relieve pain by their inherent analgesic action but exert some influence in lessening inflammatory edema in the tissues as well. Salicylate of soda or acetylsalicylic acid when used in large doses, 10 grains (0.6 gm.) may be followed by considerable amelioration of symptoms. The total dosage for twenty-four hours may be from 45 to 90 grains (3 to 6 gm.). Medication should be so spaced that the patient will have a higher concentration of the drug in the hours prior to bedtime in order that it may reasonably assure a good night's sleep. Gastric upsets from the drug may be curtailed by taking bicarbonate of soda or by use of enteric coated tablets. Sedatives such as codeine or other opium derivatives should never be used on account of addiction. Small doses of whiskey may be used instead.

Since 1925 there has been slow but gradually increasing interest shown in the use of gold salts, gold and sodium thiosulfate in aqueous suspension (gold sodium malate) are the most popular preparations. Reports in the literature are somewhat at variance with regard to total dosage. Most authors

Tuberculous arthritis may offer difficulty in differential diagnosis. Failure to demonstrate a primary tuberculous infection in the lungs or elsewhere leads to greater difficulty. Tuberculous arthritis is usually monarticular and local radiation of heat is often more marked than in rheumatoid arthritis. It may be necessary to resort to biopsy of the synovial membrane and animal inoculation before a positive diagnosis can be made.

TABLE 63

| | *Rheumatoid Arthritis* | *Degenerative Joint Disease* |
|---|---|---|
| Onset | Acute, progressive, with or without fever | Insidious, afebrile |
| Age | Any age, usually 20 to 40 years | After 40 years |
| Sex | Females 2 to 1 | Equal in both sexes |
| Weight | Underweight | Overweight |
| Joints involved | Any joint in body, usually symmetrical fusiform swelling of fingers | Spine, knees, fingers (Heberden's nodes) |
| Muscle atrophy | Marked, symmetrical | Absent or slight |
| Contractures | Marked, symmetrical | Absent |
| Disability | Frequently complete ankylosis in some joints, marked limitation by contracture and luxation | Partial through osteophytes and lipping |
| *Anemia* | *Moderate to marked* | *Coincidental* |
| Roentgen ray findings | Widening of joint space early, later atrophy of bone, obliteration of joint space | Osteophyte formation, lipping of bone, seldom atrophy of bone |
| Sedimentation of red blood cells | Rapid | Normal |

TABLE 64

| | *Rheumatic Fever* | *Rheumatoid Arthritis* | *Pyogenic Arthritis* | *Intermittent Hydrarthrosis* |
|---|---|---|---|---|
| Pressure | Increased | Increased | Increased | Increased |
| Viscosity | Slightly increased | Increased | Increased | Normal |
| Leukocytosis | Total count up to 25 000 cells, polymorphonuclear | Up to 15 000 cells, polymorphonuclear and monocytes | Up to 20 000 cells, polymorphonuclear | No increase |
| Globulin | Increased | Increased | Increased | Normal |

disease becomes spontaneously inactive after a few months, leaving little or no disability. In other patients, irrespective of treatment, the disease progresses steadily or by periods of relapse alternating with remission, resulting in widespread ankylosis of the joints and permanent disability. Generally speaking, the disease is not inconsistent with longevity, even in well advanced cases. Patients seldom die from any direct effect

Rheumatoid arthritis must be distinguished from intermittent hydrarthrosis. In this relatively benign form of chronic villous arthritis there may be slight or no constitutional symptoms. The knees are usually the only joints to become involved.

Examination of synovial fluid may be of aid in the differential diagnosis. A few examples are set forth in table 64.

*Prognosis.*—The prognosis *in rheumatoid* arthritis is variable. In some patients the

of the disease itself. Once the joints are involved, the prognosis becomes a matter of estimating the degree of disability or the return of function to the joints affected. Restoration of function to a joint cannot be expected after the cartilage has been destroyed and extensive fibrosis has occurred.

Contractures and deformities may be prevented by proper orthopedic support and the aid of a suitably trained physical therapeutist. There is hope of arresting the

active process in approximately 50 per cent of cases treated with chrysotherapy

Before outlining any plan for the treatment of rheumatoid arthritis it may be well to discuss a failure which is directly due to the physician himself Most articles dealing with the treatment of arthritis emphasize the need for rest Taken literally the patient is placed in bed and his wants cared for without so much as the elevation of his hands After months of bed rest the feet become rotated outward from pressure of the bed clothes the knees are fixed and the arms held rigidly to the sides of the body Thus the patient becomes an abject figure and totally disabled as a result of the prolonged inactivity

The treatment of rheumatoid arthritis should be carried out systematically and with careful attention to many details

The activity of the process must be gauged and methods of treatment employed to meet the individual case this applies to rest muscular activity diet physical therapy and medication

In general the patients may be divided into groups—those ambulatory and those requiring bed rest In so far as possible and with due caution for their health, we encourage patients to be ambulatory and busy This helps to keep up their morale maintain muscle tone and prevent ankylosis

The patient requiring bed-rest is usually emaciated and suffering from exquisite pain on motion of the joints Fever slight leukocytosis and moderate anemia may be present Rest for this type of patient should be relaxing in so far as possible The bed should be firm in order to avoid sagging The weight of the blankets must be kept off the feet of the patient by draping them over a wooden frame support or pillows tucked in at the foot of the bed Sand bags or partial casts may be employed to keep the extremities in good alignment and to reduce muscle spasm One or more times daily each joint should be gently flexed and extended to break down fibrous growth and prevent ankylosis The use of splints and casts for the purpose of immobilization is to be discouraged The application of such apparatus promotes ankylosis and permanent disability of a joint

Adequate nutrition must be maintained Gain in weight in undernourished patients is usually a sign of improvement whereas loss in weight offers a grave prognosis A total intake of from 2000 to 3000 calories should be encouraged depending upon the size of the patient Milk fruits meats and fish are indicated Pemberton believes there is increased absorption of carbohydrates from the intestinal tract in patients with rheumatoid arthritis and accordingly advocates the avoidance of too much starch Rinehart has shown there is a decrease in the utilization of vitamin C in patients with this disease An adequate supply of vitamin C may be insured by drinking 400 to 600 cc of fresh orange juice daily The orange juice may be supplemented by ascorbic acid preparations (*i e* cevitamic acid 0 050 three times daily) Added vitamin concentrates A B and D may aid in regaining the general nutrition of the patients

Effecting the relief of pain arising in the joints especially during the acute phase becomes a problem for the physician There is reason to believe that the salicylates not only relieve pain by their inherent analgesic action but exert some influence in lessening inflammatory edema in the tissues as well Salicylate of soda or acetylsalicylic acid when used in large doses 10 grains (0 6 gm ) may be followed by considerable amelioration of symptoms The total dosage for twenty four hours may be from 45 to 90 grains (3 to 6 gm ) Medication should be so spaced that the patient will have a higher concentration of the drug in the hours prior to bedtime in order that it may reasonably assure a good night's sleep Gastric upsets from the drug may be curtailed by taking bicarbonate of soda or by use of enteric coated tablets Sedatives such as codeine or other opium derivatives should never be used on account of addiction Small doses of whiskey may be used instead

Since 1925 there has been slow but gradually increasing interest shown in the use of gold salts gold and sodium thiosulfate in aqueous suspension (gold sodium mallate) are the most popular preparations Reports in the literature are somewhat at variance with regard to total dosage Most authors

advocate the injection of 25 to 50 mg at intervals of one week

The response to treatment may be gauged by a recession of signs of activity pain swelling local heat, fever, a return to normal of the sedimentation rate and by a general feeling of well being on the part of the patient According to the various reports these gratifying results may be expected to occur in from 50 to 80 per cent of patients so treated It may be necessary to give a third or possibly a fourth series of injections In our clinic we have adopted the plan of giving continued treatment to patients showing favorable results On the basis of these results injections are given at intervals of one month with the hope of preventing relapse

In about one-third of the patients receiving this treatment there will be evidenced a mild degree of dermatitis, and in a few patients a severe exfoliative dermatitis Purpura hemorrhagica granulocytopenia, nephritis, hepatitis may be observed, and some fatalities have been reported Examination of the urine before each injection and frequent examination of the blood are indicated

As part of the program to build up the general health of the patient foci of infection should be sought for and so far as practicable removed The tonsils paranasal sinuses gums tooth sockets gall bladder cervix and prostate should be carefully investigated and if found to be infected eradication by proper surgical procedure should be instituted Nevertheless the patient must not be led to believe that a cure will result from such a procedure

Physical therapy must be utilized as an adjunct to the medical treatment of rheumatoid arthritis This includes heat, massage passive and controlled exercise baths and a pool When properly used such measures aid primarily in the relief of pain control of muscle spasm increase in peripheral blood flow, prevention of muscle atrophy and in rehabilitation of the patient

The beneficial effect of heat on arthritic joints is well known For centuries sufferers from rheumatic pain have sought the relief afforded by natural hot springs, spas or elaborate baths In modern hospitals containing physical therapeutic equipment a variety of methods are available for promoting heat as a means of reducing pain and inflammation in the joints, these include infra red ray heat cabinets diathermy short wave baking heat pads and fever therapy

A skilled physical therapeutist can do much to prevent the development of deformities During the acute phases of pain and swelling the institution of gentle passive motion may inhibit formation of adhesions and prevent or correct contractures The loss of muscle tone and its subsequent atrophy may be minimized by massage In the later stages of the disease the correction of those deformities which may be overcome is sometimes surprising

Orthopedic measures should be employed A properly applied support to an acutely swollen joint will afford rest and relief of pain Great caution should be taken however to prevent ankylosis from prolonged inactivity Systematic exercises of muscle groups should be carried out at regular intervals throughout the day to prevent atrophy Following the acute stage removable supports may be fitted to the afflicted joints to aid the patient in becoming ambulatory or to correct contractures Braces are an essential support to the spine for the correction of kyphosis in a patient with spondylitis Occasionally surgical intervention becomes necessary to reduce contractures or possibly to free fibrotic tissue in or about a joint

In patients who are anemic, transfusions of whole blood may be the quickest and best means of restoring the red blood cells and hemoglobin to normal levels When hypochromic anemia is present iron medication (ferrous sulphate 0 3 gm three times daily) is indicated

## The Place of Cortisone and ACTH in Rheumatoid Arthritis

By John Lansbury M D

The recent introduction of Cortisone and ACTH in the management of rheumatoid arthritis has opened a new chapter in the experimental therapy of arthritis and has stimulated great interest in the possible role of steroid hormones in the pathogenesis

of the arthritides While it is too early to see the place of Cortisone in true perspective the following points are emerging —(1) Cortisone and Compound F are unique among the available steroids in their antirheumatic effect (2) This anti rheumatic effect is in no way specific but is part of a general suppressive action on a wide variety of unrelated non rheumatic diseases (3) The action of Cortisone is suppressive palliative protective and temporary It does not cure arthritis or any other disease and must for the time being be regarded as symptomatic therapy

The dramatic beneficial effects which occur immediately after the administration of cortisone or ACTH in rheumatoid arthritis must not be confused with the problem of the indefinite administration of these substances in what is generally a life long disease So far we have only a few observations on the effect of these agents on rheumatoid arthritis over a period of a year and none at all on their effect after 3 5 or 10 years Even short term administration of cortisone and ACTH is sometimes attended by undesirable and even serious side effects These are more apt to occur however in patients over 40 years of age It is probably too early to state the indications for ACTH and Cortisone therapy in arthritis Obviously they are contraindicated in the 'burnt-out' end stages of the disease Also they are contraindicated in the early cases which might respond well to gold therapy If they really have a place in treatment it would seem to be in those cases which are rapidly getting worse despite all other forms of therapy The case of moderate severity in which the patient has adjusted to his disease is best left without the false hope which Cortisone gives Short courses of Cortisone as an adjunct to straightening of knees by traction may find a place The average dose of Cortisone should not exceed 50 mg per day and both patient and doctor should accept partial rather than complete releif as their goal For this reason it is wrong to start off with large doses which give complete relief which cannot be safely maintained on a long range basis

Cortisone and ACTH are contraindicated in case of impaired myocardial function hypertension potentially psychotic personality peptic ulcer sickle cell anemia malaria and pulmonary tuberculosis

Potentially serious side effects of the agents are hydremia transient hypertension a tendency to thrombosis, hypokalemic alkalosis, delayed healing, accentuation of diabetes mellitus and alternating states of mania and depression In long-continued cortisone or ACTH therapy there is theoretically, danger of pituitary and/or adrenal cortical atrophy and lowering of thyroid function (as judged by the reduction of protein bound iodine levels of the blood and reduced radio active I uptake) There is also danger of increased serum-cholesterol levels with the possibility of premature atherosclerosis (as seen in spontaneous Cushing s syndrome) and perhaps osteoporosis There is some evidence of a decline in response to both ACTH and cortisone over a long period

Annoying but not necessarily serious side effects have been reported as follows renal glycosuria obesity increased tendency to infection salivation changes in auditory function (impairment or increased acuity) blurred vision weakness acne moon face of Cushing s syndrome and a tendency to fractures in old people a tendency due either to increased activity or to an increase in osteoporosis

Cortisone and ACTH if warranted at all in the treatment of rheumatoid arthritis should certainly be reserved for rapidly progressing cases that have failed to respond to other measures (such as gold therapy) Patients receiving these agents should have their sodium intake limited to 200 mg a day should receive additional potassium in the form of either potassium acetate or chloride (in doses of from 1 to 5 grams a day) should note their daily basal weight in order to detect early water retention and should have a weekly record of blood pressure until their pressor response is known to be within safe limits An electrocardiogram and a determination of the sodium and potassium levels of the blood may also be of value in detecting potassium depletion and sodium retention

The hydremia by far the most common complication may be partly controlled by the program given above Diuretics in the

form of ammonium chloride and mercurials (the latter used *periodically*) may assist in controlling the water retention Some authors mention the use of thyroid substance and of estrogens and testosterone to help combat some of the side effects but further observation is required before these can be regarded as standard therapeutic agents Electroshock therapy may reverse the depression sometimes caused either by cortisone administration or by cortisone withdrawal

There is reasonable hope that modifications in the technique of administration of Cortisone and of Compound F or perhaps the use of synergistic drugs may eventually permit the use of much smaller doses so that the undesirable side effects of these steroids *may be lessened to the extent of making* their long range use in arthritis safe and satisfactory

In their present state they must be regarded as experimental rather than as an established therapy

## Degenerative Joint Disease

*Synonyms* — Hypertrophic arthritis Osteo arthritis

*Definition* — Osteo arthritis is an arthropathy of unknown etiology, principally affecting *middle-aged or elderly persons* The joint deformity results from loss of cartilage and absorption of bone hypertrophy with lipping and osteophyte spur formation at the joint margins

*Etiology* — There are perhaps many factors which contribute to the joint changes in osteo-arthritis The process of aging itself renders changes in the bony tissues that make them less resistant to the stresses and strains to which they commonly are subjected

Vascular degeneration with its diminished blood supply, osteoporosis and loss of elasticity of cartilage break down the resistance of the tissues to trauma and postural strain Perhaps these changes may be considered metabolic in nature and it may be that infection does not enter into the production of this disease Hypertrophic changes sometimes are found in joints as a late manifestation of traumatic gouty, hemophilic gonorrheal or rheumatoid *arthritis* and may be considered as secondary changes

Since no infectious agent has been found as the causative principle and since the joint changes are *not those typical of an inflam*matory reaction, it hardly seems consistent to use the term "arthritis" in referring to this condition The American Rheumatism Association recommends the term "osteoarthritis", therefore, it shall be used here in accordance with their classification The term degenerative joint disease would seem to bear more relevancy as a classification for this particular group

*Pathology* —The changes characteristic of osteo arthritis develop slowly over a long period of time Bennett, Waine and Bauer have *studied the histological development* of the disorder in a series of 60 presumably normal knee joints They found the earliest trace to be present in the third decade of life The cartilages most likely are first to show the process of degeneration Early there is absorption of central areas of the cartilage or about the periphery and later the cartilage may be entirely absorbed An attempt at repair is visible in the formation of small amounts of fibrous tissue and spongy bone structure At the edges of the joint bony formation is more advanced and there are *rounded prominences of spongy* bone covered by cartilage These take on the appearance of lipping or spur formation The ends of the shaft of the bone become porous and its articular surface is eburnated and polished

In the periarticular structures there is little or no evidence of the inflammatory swelling so characteristic of rheumatoid arthritis However ossification which presumably is part of the degenerative process may be seen in the tendinous insertions and in the ligaments and bursæ The skin seldom shows any change The synovial membrane may be thickened especially about the periphery Within the synovial cavity fragments of bone or cartilage may break off or be eroded off to form loose bodies These are the so-called *joint mice* Ankylosis of a joint does not occur but there may be locking of a joint due to loss of cartilage and the interference of its

motion due to lipping or spur formation

The study of the distribution of these pathologic changes throughout the body is of interest The spine knees and hips are most often affected These are the weight bearing joints and those most subject to postural strain In the terminal phalangeal joints may be found bony enlargements which are pathognomonic of hypertrophic arthritis These are known as Heberden s nodes

A rough estimate has been made that 90 per cent of the general population over fifty years of age show some evidence of hyper trophic arthritis The processes are seen during routine roentgen ray examinations and more often than not are asymptomatic Their presence usually is unknown to the patient A very small percentage of individuals may complain of symptoms arising from hypertrophic joint changes

*Osteo-arthritis (Degenerative Joint Disease) of the Cervical Vertebræ* —In recent years a syndrome characterized by pain about the neck and in the shoulder girdle has been the subject of considerable discussion In the medical literature one finds such conditions designated as radiculitis pain of nerve root origin neuritis or the radicular syndrome as described by Gunther and Kerr

Mettier and Capp studied a group of patients with symptoms characteristic of cervical arthritis The symptoms com plained of most frequently were pain rigidity of the neck and muscular weakness of the hand or arm The onset of pain was usually abrupt and in many cases was first noticed by the patient on awakening in the morning More often than not the pain was localized in and about the shoulders especially about the insertion of the deltoid muscle or it radiated down the arm into the fingers As a rule these symptoms ap peared months or even years before there were any complaints of discomfort in the region of the neck Usually the pain is *unilateral but with* the exception of a few instances it becomes bilateral at some time during the progression of the pathologic condition The pain varies from that of an excruciating character to a dull aching sensation At times it is described as sharp jabbing needle like and penetrating at other times as a prickly or stinging feeling Some patients complain only of numbness and tingling in the fingers or of a drawing or dead aching sensation in the muscles of the arm

The loss of freedom or use of one upper extremity is a common complaint Many patients become unable to comb their hair or to extend the arm behind the back to adjust their clothing Others are unable to perform fine movements such as sewing or writing and some of them find it difficult to grasp objects

A few patients become conscious of pain in the neck during the early course of illness but in most patients it is a late development In no instance is there definite restriction of movement of the head and neck but it is often stated that pain in the neck may be induced by jarring of the body The dis comfort is sometimes described as a head ache at the base of the brain as a feeling of ' congestion at the base of the brain or simply as muscular soreness

There is no evidence of atrophy of the muscles of the hands arms or shoulder girdle The reflexes of the arm show normal reactions

Roentgenographs taken of the cervical vertebræ should include exposure of the oblique as well as the usual anterior pos terior and lateral projections Hypertrophic changes from slight to marked may be observed such changes as circumferential osteophyte formations These project into the intervertebral canals from the superior or inferior margins of the vertebræ and cause narrowing of the foramina Osteo-arthrosis occurs more frequently on the left side than on the right In addition the intervertebral disks are usually thinned out in the region of exostosis It is an interesting fact that the sites of predilection are distributed between the fifth and sixth and the sixth and seventh vertebræ X-ray findings may be minimal at first and appear more striking after symptoms subside

In the differential diagnosis one must give consideration to such conditions as trau matic injury to the brachial plexus or to pressure on this structure by cervical ribs or hypertrophied scaleni muscles (scalenus anticus syndrome) actual destruction of the

vertebra by bacterial agents or neoplastic metastasis, and traumatic arthritis of the shoulder joint and bursitis

*Hypertrophic Spondylitis* —Evidences of osteo arthritis also may be found in the thoracic vertebræ but especially in the lumbar vertebræ A ring of osteophytes around the joint gives the characteristic roentgen ray picture There is relatively little pain accompanying these changes although occasionally there may be radiculitis There is never the complete ankylosis of the Marie Strumpell type have considerable difficulty in going up and down stairs Aches and pains in the ham string the gastrocnemius and peroneal groups of muscles frequently bring forth complaints

There are relatively few findings on physical examination Slight swelling of the afflicted knee may be apparent the changes are usually more pronounced in one knee than the other but may be symmetrical There is slightly increased warmth of the skin, but this is not as pronounced as in rheumatoid arthritis On careful examina-



FIG 219 —Degenerative joint disease hypertrophic arthritis of cervical vertebræ

*Osteo-arthritis of the Knees* —The symptoms arising from hypertrophic arthritis of the knees usually come on slowly In the early stages there may be slight pain and stiffness but as the process becomes more advanced pain and stiffness become increasingly severe The symptoms are most marked when the patient begins to move about after a period of rest On arising from bed or on attempting to get up from a chair action in the knee joint is inhibited by pain and stiffness After limping about and exercising for a short time the symptoms subside and the patient may resume a fair degree of activity These patients usually tion of the joint margin with the palpating finger definite points of tenderness may be localized A grating sensation or crepitation may be felt when the palmar surface of the hand is placed on the patella and the leg flexed or extended on the thigh

Examination with the roentgen ray will reveal many characteristic findings Degeneration of the cartilage is discernible and narrowing of the joint space is apparent Irregular destruction and hypertrophy of the marginal bone is seen evincing a picture of bony overgrowth lipping and spur formation

*Osteo-arthritis of the Hips (Hip joint disease of the aged Morbus coxæ senilis Malum coxæ senila)* —Osteo-arthritis of the hips it may be truly said is an excellent example of degenerative joint disease Trauma incident to obesity or external blows is a most important precipitating factor Often on careful questioning it is elicited that the patient had sustained an injury of one sort or another to the hip joint years before the onset of symptoms This type of joint disability is not infrequently seen in patients with Paget s disease

The structural changes in the joint are largely consistent with a loss of cartilage, especially in the weight bearing regions There is eburnation of the surrounding bone Fixation of the joint may result from roughening of the articular surface and flattening of the head of the femur As the process advances the fossa of the acetabulum becomes enlarged and deepened

The onset of symptoms comes on insidiously The patient may first experience some stiffness and pain in the thigh At this stage an erroneous diagnosis of 'sciatica may be made After a period of weeks or months a limp becomes noticeable and pain is induced by motion Pain and disability progress and become outstanding symptoms The patient finally resorts to the use of a cane seldom to crutches

Shortening of the leg occurs as a result of the narrowing of the joint space and becomes further accentuated by the deepening of the acetabulum The patient assumes a stooped posture He walks with a rolling limping gait and depends upon his cane for considerable support

On examination atrophy and spasm of the regional muscles are observed Motion of the joint is limited in all directions There is usually no impairment of the reflexes

Examination of the roentgen ray film discloses narrowing of the joint space however there is little or no evidence of cartilage In the surrounding bone increased density is seen due to eburnation The characteristic changes of osteo-arthritis are apparent about the joint margins where lipping and spur formation have taken place

*Heberden s Nodes* —Heberden s nodes are bony swellings which appear at the terminal phalangeal joints They are usually symmetrical and not associated with pain Some discomfort may be noticed because of interference in freedom of motion of the joint or soreness resulting from trauma to the vulnerable projections In a well advanced case there may be some angulation and fixation of the terminal phalanx

This condition is readily differentiated from rheumatoid arthritis In the latter, the middle interphalangeal joint is usually involved and shows the characteristic fusiform soft tissue swelling The bony outgrowths at the terminal phalanges are frequently confused with gout especially in the minds of the laity Tenosynovitis or localized bursitis may simulate the Heberden s node Such foci of tenosynovitis will show evidences of an inflammatory reaction Heat, redness and tenderness are sufficient findings to make a differential diagnosis

*Menopausal Arthritis* —A definition of ' menopausal arthritis will not be attempted here because there is insufficient evidence to indicate that this is a clinical syndrome however some observers believe the disturbance is primarily endocrine in origin

During the menopause women not infrequently become conscious of pain and aches in or about the joints An early manifestation may be an audible creaking sound when the patient kneels On examination the knee joints are most often observed to be affected The regional findings are those characteristic of osteo-arthritis Occasionally there may be hypertrophy of the synovial villi and effusion in the synovial sac Most women are overweight in a degree disproportionate to their bony and ligamentous structure as a result there may be evidences of joint strain in the feet ankles hips and back Pes planus puffiness about the ankles stiffness in the hips and poor posture also may be found in varying degrees

*Treatment* —Middle aged or elderly patients complaining of stiffness and pain in or about the joints repeatedly come to the physician with the conviction that they are about to become hopelessly crippled from arthritis Should the symptoms prove to arise from osteo-arthritis (degenerative joint disease) it is important to acquaint the

patient with the nature of his condition He should be informed that this is an infirmity which is mainly the result of the aging process and of repeated trauma to the articular structures through joint strain It should not be confused with the disability found in connection with progressive ankylosis of the joints as manifested in rheumatoid arthritis Reassurance of the patient that he will not progress to total disability is often enough to bring forth the expression, I feel greatly relieved already! A person beyond the age of fifty to whom it is explained that he or she is approaching middle age usually will understand these changes

Patients with osteo-arthritis should not be encouraged to remain in any fixed position for a long period of time In osteo arthritis of the knees and hips prolonged sitting promotes muscle spasm and stiffness Periods of rest alternating with exercise should be planned Elevation of the legs or flexion and extension of the legs on the thighs at frequent intervals is often sufficient to keep the lower extremities limbered up

Relief of pain is essential An analgesic drug such as acetylsalicylic acid when properly used is often sufficient to produce satisfying results This drug will relieve pain when given in divided doses so that the patient receives from 3 to 4 grams throughout a twenty four hour period Patients who are freed of these painful symptoms will regain confidence and the courage to use their extremities However caution must be observed in giving large doses of acetylsalicylic acid to elderly patients with cerebral arteriosclerosis occasionally a drop in blood pressure may occur

Obesity is frequently encountered in patients with osteo arthritis of the knees (menopausal arthritis) and hips and is an indication for reduction in weight

Various mechanical supports for the joints may be required Elastic supporters for the knees, braces for the hips and back will be found valuable A board under the mattress to avoid bowing of the springs may help to correct back strain

Relief of pain and stiffness may come from the use of physical therapy in the form of heat and light massage Baking diathermy or such simple household procedures as the application of wet packs or a well covered hot iron to the involved joint may prove effective The patient, or a member of the household can be taught to massage gently the articular structures Alcohol warm oil, or a liniment (equal parts of methyl salicylate and chloroform liniment) may serve as an external lubricant

Patients with hypertrophic spondylitis will require particular attention and instruction Correction of posture becomes paramount and can best be done by a trained physical therapeutist This applies not only to lumbar strain but to cervicodorsal kyphosis as well In cervical osteo-arthritis gentle manipulation of the vertebræ and manual traction may be beneficial in addition to massage

### Arthritis of Immediate Traumatic Origin

Traumatic joint disease may result from a single blow or fall, or from repeated slight trauma to the articular structures Disability may occur immediately or not until months or years have elapsed following the initial injury

In acute traumatic arthritis joint function is disturbed as a result of sudden torsion or a blow such as may be experienced in playing football or in a fall The knee joint is most frequently involved There may be an internal derangement resulting from damage to the semilunar internal or lateral cartilages The knee joint becomes locked and synovial swelling soon appears Sprain of the ligamentous supports of the knee or other joints may produce tears and coincidental rupture of blood vessels with hemorrhages in the tissues A common form of acute traumatic arthritis results from injury to a distal phalanx Rubbing of an elongated nail of the big toe against the shoe stubbing the toe against a fixed object or a blow from a baseball on the end of a finger may induce sufficient concussion to injure the delicate synovial tissues

In the chronic form of traumatic arthritis the initial injury which produced transient disability and seemed entirely inconsequential at the time may reappear months or even years later when the patient will

become aware of the insidious development of pain and stiffness

Often the symptoms may come on so insidiously or at a period so far distant from the original trauma that the patient may completely fail to recall an injury or do so with some difficulty Other inceptive causes may be a blow to the shoulder sustained in an automobile accident a fall down stairs striking the coccyx (coccygodynia) or repeated sprain of a wrist or ankle leading to chronic changes

*Definition* —Gout is presumably a disturbance of purine metabolism The clinical manifestations are characterized by severe pain in articular structures and the formation of tophi It is a chronic condition with a tendency to acute attacks

The history etiology pathologic physiology and treatment are considered in the section on diseases of metabolism page 505

*Course of Illness* — The first attack of gout usually appears at the site of the metatarsophalangeal joint of the great toe and most

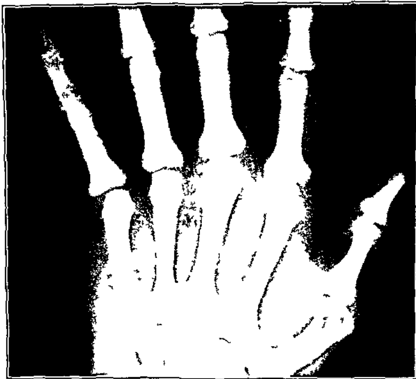


Fig 220 —Gout Note punched out areas in terminal portions of proximal phalanges

The structural alteration in affected joints is essentially that of osteo arthritis Loss of cartilage lipping and spur formation are *the characteristic findings*

It may be mentioned here that trauma may be a precipitating factor in other types of joint disease

## Arthritis of Gout

*Synonyms* — Gouty arthritis Podagra Metabolic arthritis

often is monarticular However the instep heel ankle knee and in rare instances the fingers or wrist may show the first signs of the disease Pain is the outstanding symptom noted by the patient and usually appears suddenly at night At the onset it is dull and aching in character but after several hours it becomes a constant and excruciating aching sensation The surrounding soft tissues are red and swollen and the regional veins are dilated The joint is extremely sensitive to touch or pressure The reaction of the

initial attack begins to lessen after two or three days. The hyperemia subsides, the tissues become less sensitive and painful but a moderate degree of edema persists.

Following the first attack of gout there may be a recurrence of the illness in from two weeks to as long as two years. With the passage of time there is a tendency for the attacks to occur at more frequent intervals.

Clinically, a chronic state of gout is recognized. The patient is usually obese, but may be thin, he has a florid complexion and is reputed for his excesses in fatty foods, red meats and wine. The insatiable desire for rich, highly seasoned foods often becomes acute just prior to a flare up of joint symptoms. One or more tophi are seen on the auricula of the ears. There is persistent slight swelling, redness and tenderness of the involved joint. There even may be bony ankylosis. The roentgen ray picture usually is unmistakable. Deposits of sodium urate crystals may be seen in the cartilages and synovia. There may be marked destruction of the cartilage. Bony overgrowth and spur formation is not an unusual finding. In the region subjacent to the cartilage bone is absorbed and replaced by gouty deposits appearing as dense rounded shadows on the film. These punched out areas are 3 mm or more in diameter and are characteristic of advanced gouty arthritis.

Swelling of the olecranon bursa is frequently seen in chronic gout.

Although these changes are more or less paramount the patient may follow the pursuit of his duties relatively free of symptoms when there will be a sudden and acute exacerbation of joint swelling accompanied by pain. Such episodes may be precipitated by trauma. Overexercise and sweating, chill or swimming in cold water may bring on an exacerbation. It is not unusual for an attack of gout to appear within a few hours after a surgical operation. Just prior to the attack the patient develops a craving for fatty food and is irritable and cranky. Gout is always a chronic condition with a tendency to acute attacks (Hench).

## Arthritis of Neuropathic Origin

*Synonyms* —Charcot's joint. Trophic arthritis.—In untreated syphilitic patients with tabes dorsalis, a type of arthropathy occasionally is seen. The first clinical description was given by Charcot in 1868.

The knee joint is most frequently involved. The changes are essentially trophic in nature. There is marked absorption and disintegration of bone irregularly distributed throughout the portions entering into the formation of the joint. Adjacent to such areas there

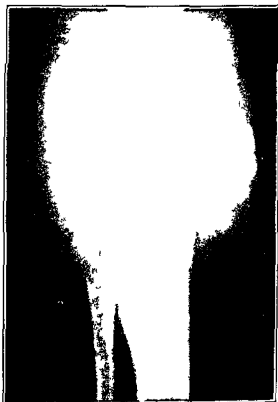


Fig 221 —Charcot's joint

is new bone formation. The process of destruction and the building of new bone give the joint certain characteristics that render these changes clinically recognizable. There may be enormous enlargements of the bony outline of the joint causing the joint to feel like a sac of bones. Ankylosis does not occur. The skin overlying the joint is thin and glossy.

Pain is sometimes experienced, but characteristically there is lack of pain or tenderness. The patient exhibits hypermotility of the joint to a marked degree without experiencing discomfort.

Syringomyelia shows arthropathies of a somewhat similar nature wherein the shoul

der and elbow frequently are involved Both syringomyelia and tabes affect the feet

Arthritis due to nerve injury or in connection with hemiplegia or chronic encephalitis may be of varying types

## Neoplasms of Joints

Neoplastic processes arising from joint structures are relatively uncommon

Osteochondroma —This is a relatively benign swelling which may appear along the joint margin or at the distal end of a bone It is most often seen in persons between twenty and fifty years of age The symptoms are relatively mild, usually in the form of an aching sensation Pressure or soreness from trauma may attract the patient's attention to a small palpable, hard swelling The histologic examination reveals a chondromatous mass in which there are areas of calcification and ossification These small tumors usually may be detected by the roentgen ray and are recognized by a bony projection through the periosteum the tip of which is covered by cartilage

Synovioma — *Synonyms* —Fibrosarcoma Synovial sarcoma —The synovioma is a sarcomatous degeneration of the synovial membrane Cases occurring in early infancy and the aged have been reported in the literature The tumor may be slow growing and relatively benign or highly malignant A dull aching pain and joint swelling are the outstanding symptoms It is monarticular in distribution The tumors are not sensitive to the roentgen ray Radical excision must be resorted to The prognosis is poor

## Miscellaneous Forms of Arthritis Associated With Other Diseases

Intermittent Hydrarthrosis — *Synonyms* —Chronic villous arthritis Chronic synovitis —This is a chronic disorder of the joints usually the knees and is characterized by a gradual onset of stiffness and swelling with a tendency to remissions and exacerbations

*Etiology* —The evidence for a specific infectious agent as the cause of this disorder is less convincing than for other forms of arthritis Various forms of bacteria have been isolated from the synovial fluid of these joints including the Brucella abortus however none seems of etiologic significance It appears most often in persons between the ages of twenty and forty five There does not seem to be an hereditary factor Although the disease occurs in both men and women some authors believe it to be of more frequent occurrence in women Trauma apparently is not a factor

*Pathology* —The reports concerning the histologic changes in this condition are few in number The synovial villi become elongated and hypertrophied The tissues appear edematous and there may be an infiltration with lymphocytes In the late stages some of the synovial fringes may become broken off and are seen as foreign bodies in the joint space There is little or none of the cartilaginous degeneration or pannus formation so characteristic of rheumatoid arthritis

*Symptoms* —The knee joints are most frequently involved, but evidences of intermittent hydrarthrosis may appear in the metacarpophalangeal and interphalangeal joints The onset of symptoms is gradual At first the patient is conscious of stiffness in a single or in symmetrical joints Swelling gradually appears and slowly progresses until the synovial sac is well distended The patient complains of discomfort and later of considerable pain Signs of inflammation local redness and heat are lacking but there is no fever or leukocytosis There is interference of the functional ability of the involved joint due to its being markedly swollen

The attack may last for several weeks before the effusion disappears The swelling may subside completely or there may be a permanent residual of swelling Subsequent attacks may occur at intervals of several weeks or months

After repeated attacks the patient becomes subject to permanent disability due to the proliferation and marked excess of villous tissue in the joint cavity

Roentgenograms show widening of the

joint space The bones show little or no change the outline of the bone remains smooth and clear within the joints and the cartilage is not obliterated

*Treatment* —Analgesic drugs may relieve the pain but will have no effect on the progress of the disease Rest is indicated in order to minimize trauma to the joint

Elastic supporters applied to the knees help to support the legs and suppress further effusion

It is reported that surgical treatment has given good results the joint is opened and the redundant synovial tissue removed Favorable results have also been recorded following roentgen ray therapy to the joints

HEMOPHILIC ARTHRITIS —*Synonym* —Hemarthrosis —One of the relatively frequent complications of hemophilia is the tendency to hemorrhage into the joints The clinical aspects of hemophilic arthritis have been reviewed by Key Keefer and Myers Recently, McDonald and Lozner reported on the roentgenographic findings in hemophilic arthritis Two stages are recognized (1) acute hemarthrosis and (2) the stage of healing chronic hemophilic arthritis

In *acute hemarthrosis* there is rapid swelling of the joint due to extravasation of blood within the capsule Rather severe pain accompanies the distention of the synovial sac and function of the joint is inhibited depending upon the degree of swelling The overlying skin is not red and there may or may not be slight increase in local heat The knees hips fingers and toes are the joints most frequently involved

A history of trauma sprain or torsion to the joint usually is elicited The patient is subject to repeated attacks involving the same or other joints This abnormality



FIG 222 —Hemophilic arthritis There is loss of cartilage ankylosis of the joint and marked atrophy of the bones

usually appears in the hemophiliac during childhood but has been reported in the fifth and sixth decades There is a decreasing tendency toward hemarthrosis with age presumably due to the accompanying lessened activity

The roentgenograms merely show distention of the joint cavity

The *treatment* consists of absolute bed rest and protection of the joint from motion or further trauma

Following the acute attack absorption of the suffused blood may occur leaving comparatively little disability

In *chronic hemophilic arthritis* there is a tendency to repeated hemorrhage into a single joint Due to failure of complete absorption of the blood there are evidences of attempts at organization and repair Fibroblastic proliferation is apparent and ankylosis of the joint results Accompanying this phenomenon there is some periarticular swelling and muscle atrophy becomes marked The joint becomes permanently enlarged and tender to the touch Contractures of the muscle develop and the extremities become deformed

In the roentgenograms the early changes are characterized by destruction of cartilage the appearance of spurs at the margin of the joint and slightly increased periarticular density As the process advances there is slight narrowing and irregularity of outline of the joint space Cysts appear in the subchondral tissue Finally there is marked narrowing of the joint space the articular surface is irregularly indented and the ends of the bones become deformed and decalcified There is marked subchondral cystic formation

Chronic Septic Joints —Chronic septic joints are due to localization of bacteria in or adjacent to a joint itself These foci are usually secondary metastases of organisms from elsewhere in the body The process is characterized by tissue destruction and usually the formation of pus Chronic draining from the sinuses may develop The causative agents are usually the tubercle typhoid and colon bacilli rarely are they staphylococci gonococci streptococci meningococci or pneumococci

The Oidium coccidioides (coccidioidal granuloma) may invade the bony tissues about an articular surface The infection simulates tuberculosis The spores enter the blood stream from foci in the lungs or soft tissues and invade the bones There is much destruction of tissue followed by the formation of a chronically draining sinus

*Madura foot* is endemic in India however 30 cases have been observed in North America The lesions involve the soft parts and bone especially of the foot The causative organism is thought to be a fungus

Allergic Arthritis —Acute swelling of a joint is not uncommon as an accompaniment to serum sickness Many joints may become involved especially the knees elbows wrists interphalangeal and shoulder joints Effusion into the synovial sac occurs rapidly and causes considerable pain The joints may show marked swelling or redness and are exquisitely tender These manifestations of abnormal reaction to serum usually subside spontaneously and rapidly

As a rule other signs of serum sickness are present such as urticaria and a high eosinophil count

Sedatives injections of adrenalin and cool applications applied locally may aid in relieving the patient s discomfort

## REFERENCES

### *Diseases of the Joints*


For reports on literature relative to Arthritis the reader is referred to the Reports of the Editorial Committee of the American Rheumatism Association

Committee for the Eighth Rheumatism Review Hench P S Bauer W Boland E Dawson H Freyberg R H Holbrook P Key J A Lockie M McEwen C

Rheumatism and Arthritis Review of American and English literature for 1940 (Eighth Rheumatism Review) Ann Int Med 1941 December

Rheumatism and Arthritis Review of American and English literature of recent years (Ninth Rheumatism Review) Ann Int Med 1948 January and February

These reviews offer a full bibliography of articles published in the English language classified and discussed with pertinent editorial comment

Bauer W and Short C L The Treatment of the Arthritis of Known Origin New England Jour Med 1940 223 286

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structures or muscular aponeuroses in regions where pressure may come to bear on nerve bundles or trunks. Sir Thomas Lewis demonstrated a radicular type of pain that followed the injection of sterile salt solution in ligamentous and tendinous attachments to the vertebral processes. When the lower cervical or upper thoracic segments were irritated, the pain induced closely simulated that of angina pectoris. Recently Inman and Saunders stated that damage to ligamentous structures in connection with the lumbar vertebræ could act as a focus of irritation to the related nerve bundles and give rise to the sciatic radiation of pain.

Although fibrositis may not be generally accepted as a distinct entity, the results of some experimental work are beginning to appear in the medical literature establishing the relationship between ligamentous structures and radiation of pain over the course of the nerve trunks. The origin of fibrous tissue hyperplasia may in some way be related to congenital, traumatic, infectious, postural and other agents.

*Treatment.*—The immediate treatment is essentially symptomatic and is centered on giving the patient relief. The salicylates, sodium salicylate or acetyl salicylic acid, offer the greatest benefit. Such drugs are of value not only for their analgesic effect but because they tend to reduce swelling as well.

Local heat (hot packs, infra red rays), radiant heat (carbon filaments) or diathermy helps relieve pain. Massage or muscle stimulation by faradic current or other physical therapeutic measures may be indicated to overcome joint stiffness and to prevent contractures.

Measures to relieve postural strain, prevent trauma, and improve the patient's general health should be given proper consideration.

## Localized and Special Forms of Fibrositis

Localized hyperplasia of fibrous tissues may be encountered in connection with various diseases and in various locations throughout the body. It is not uncommonly seen in patients with rheumatoid arthritis and other conditions affecting the locomotor system.

Special forms of fibrositis may be classified as follows:

- Palmar fascia—*Dupuytren's contracture*
- Fibrous reticulum of the panniculus adiposus—*panniculitis*
- Nerve sheaths—*perineural fibrositis*
- Joint capsule—*capsular rheumatism*
- Fibrous tissue of muscle bundles of sheaths—*intramuscular fibrositis (interstitial myositis, muscular rheumatism, myalgia)*
- Bursæ—*bursitis*

## Dupuytren's Contracture (Fibrositis of the Palmar Fascia)

This is a common example of fascial fibrositis appearing in adults, usually at middle age although it may appear as early as the third decade. It is much more common in men than in women and it is usually found in one hand although it may be bilateral. The course of illness is gradual and after a period of time the local findings are characterized by contracture of the palmar fascia causing flexion of two or three fingers on the ulnar side of the hand. The fascia becomes adherent to the skin. The fibrous nodules are palpable and may appear as an early sign of the disease. Dimpling and deep creasing of the skin are characteristic. The degree of flexion contracture increases with the passage of time and the greatest involvement is shown in the little finger. The intensity of contracture decreases with each finger as the radial side is approached; the index finger is seldom affected.

The cause of this regional fibrositis is obscure. Treatment is surgical.

## Panniculitis.—*See* Chapter 11

## Bursitis

The bursæ are small sacs widely distributed wherever friction between muscle bundles and tendons occurs. They are made essentially of fibrous tissue. The central cavity of some of these is lined with a synovial like membrane and filled with fluid. These sacs become the locus of an

Ellman Phillip Lawrence J S and Thorold G P Gold Therapy in Rheumatoid Arthritis Brit Med Jour 1940 *II* 314

Hollander J L *et al* Arthritis and Allied Conditions ed 4 Philadelphia Lea & Febiger 1949

Klauder J V and Robertson H F Symmetrical Serous Synovitis (Clutton s Joint) Jour Am Med Assn 1934 *103* 236

Mettier S R and Capp C S Neurological Symptoms and Clinical Findings in Patients with Cervical Degenerative Arthritis Ann Int Med 1941 *14* 1315

Nichols E H and Richardson F L Arthritis Deformans Jour Med Res 1909 N S 16 149

Rinehart J F and Mettier S R The Heart Valves and Muscle in Experimental Scurvy with Superimposed Infection Am Jour Path 1934 *10* 61

Soto Hall R and Haldeman K O The Diagnosis of Neuropathic Joint Disease (Charcot Joint) Jour Am Med Assn 1940 *114* 2076

Still G T On a Form of Chronic Joint Diseases in Children Med Chirurg Soc Trans London 1897 *80* 47

Williams A Justin Rheumatoid (Marie Strumpell) Spondylitis Calif Med 1949 *70* 257


## DISEASES OF THE FIBROUS TISSUES

### Fibrositis

Stockman s definition of fibrositis is "a condition of chronic inflammation of the white fibrous tissue of the fascia aponeuroses sheaths of muscles and nerves ligaments tendons periosteum and subcutaneous tissue occurring in all parts of the body, and giving rise to pain aching stiffness, and other symptoms the result of preceding general infections or of local inflammation or injuries

### Primary Fibrositis

Primary fibrositis is relatively common Its symptoms arise from a chronic inflammatory reaction within the fibrous tissue of muscle sheaths and many kinds of mesenchymatous structures It accounts for many of the conditions designated as chronic arthritis 'muscular rheumatism," peripheral perineuritis, lumbago, sciatica, 'neuralgia and some types of torticollis

*Etiology* —The cause of primary fibrositis is unknown It may first appear during the course of acute rheumatic fever or some other infectious disease having the general manifestations of a toxemia Other factors which may be concerned in the development of this little understood condition are recurrent acute respiratory infections or chronic focal infections Undue exposure to cold weather and dampness, prolonged fatigue occupational hazards, muscular and ligamentous strain and malnutrition all may play a part in producing the inflammatory reaction in the fibrous tissues

*Pathology* —According to Stockman, the structural changes are confined to the white fibrous tissue There is a proliferation of fibroblasts within the connective tissue and an absence of *leukocytic infiltration* The tissue tends to undergo organization and there is an ingrowth of newly formed capillaries These changes may be found in areas widely distributed throughout the body or restricted to certain regions After varying periods of time the inflammatory hyperplasia may subside but in most cases the reaction becomes more desmoid and permanent These fibrous indurations assume various forms Although large areas may become thickened in the lumbar aponeurosis or fascia lata they more commonly take the form of *small circumscribed structures varying in* size from a few millimeters to 1 or 2 centimeters

*Symptoms* —Pain is the outstanding symptom This may be described as a dull aching sensation sometimes constant at other times intermittent in character The activity of muscle and joint structures may be inhibited The nature of the pain and the degree of disability depend largely on the regions involved whether in relation to joints muscle fibers ligaments or nerve trunks When periarticular structures are involved the symptoms may simulate those of rheumatoid arthritis and there may be considerable disability The involvement of tendons may be recognized by muscle weakness and the finding on palpation of small hard 'pea sized nodules within the fibrous structures near the region of bony attachment Evidences of *nerve irritation* are seen in connection with hypertrophy of ligamentous

*of an intervertebral disk* may give rise to lumbar pain. In long standing cases spinal curvature results; however, there is an associated sciatic distribution of pain and the knee jerk and Achilles tendon reflexes may be depressed or absent. The characteristic finding of rupture of the contents of the disk into the spinal canal may be seen in roentgenograms taken after the intrathecal injection of lipiodol. Sacro-iliac strain may cause spasm of the lumbar muscles. Pain is relieved following the application of a well fitting belt that firmly fixes the pelvis. Spondylolisthesis, tumors of the lower segments of the spinal cord and neoplastic growths infiltrating the sciatic nerve trunk give rise to symptoms that are radicular in distribution along the ramifications of the sciatic nerve. Metastatic carcinoma of the spine, Pott's disease of the vertebræ and osteo-arthritis will be revealed by roentgen ray examination. Paget's disease and plasma cell myeloma also must be given proper consideration in the differential diagnosis.

*Treatment.*—An attempt should be made to reduce the muscle spasm. This may be accomplished by administering large doses of analgesic drugs at stated and frequent intervals. Capsules containing acetylsalicylic acid (5 gr. 0.3 gm.) combined with codeine sulphate (¼ gr. 15 mg.) may be given the patient every two to four hours depending upon the severity of the case. It may even be necessary to give two capsules for the first and second doses. (The dosage recommended here may be compounded in a number 1 capsule that is of convenient size and easy to swallow.)

Local application of heat, hot packs or hot water bottle, followed by vigorous massage help to allay mild attacks within a few hours.

Radiation by the roentgen ray may be beneficial. An acute flare up of symptoms may result from the first treatment; subsequent treatment may bring relief.

A person once having an attack of lumbago is subject to a recurrence. He should be instructed to avoid straining, stooping, heavy lifting and exposure to cold in an attempt to prevent such an occurrence. A chronic state of lumbago accompanied by persistent pain and stiffness may result from repeated recrudescences.

*Treatment* of chronic lumbago is difficult and usually requires the aid of the orthopedic surgeon.

STERNOCLEIDOMASTOID MUSCLES (*Torticollis. Wry Neck*).—In this condition the head is drawn to one side. The abnormal position is more or less fixed and permanent. Torticollis is of relatively common occurrence. The etiology is little understood. Some cases of torticollis may be functional in nature resulting from psychosomatic imbalance. In addition to fibrositis an infiltration of lymphocytes within the muscle fibers has been described.

TRAPEZIUS MUSCLES (*Trapezius Myositis*).—Trapezius myositis is characterized by pain and stiffness in the trapezius muscle on one or both sides. The pain usually is not severe and may be described by the patient as a soreness in the muscles. The pain may radiate into the suboccipital or shoulder regions.

This affection commonly occurs in association with upper respiratory infections. Repeated attacks of the common cold, chronic inflammation of the nasal accessory sinuses, especially the ethmoid, may be predisposing factors.

Local examination of the trapezius muscles reveals few findings. Motion of the neck or shoulder girdle may be limited. The muscle bundles may feel tense and pain is elicited on pressure. There may be hyperplasia of the regional lymph nodes. A few firm tender nodules may be felt deep within the muscle substance.

Local measures are important in the treatment of trapezius myositis. At first the patient may be given an analgesic drug. Heat and deep massage will aid in the relief of pain and muscle spasm. Later manipulation may be required to relieve stiffness.

EPIDEMIC DIAPHRAGMATIC PLEURODYNIA (*Devil's Grip*).—This condition is of relatively rare occurrence in the United States. A few cases have been reported in the Mississippi Valley and the state of Colorado. Recent studies indicate that coxsackie virus of type B is of definite etiologic importance.

The onset of illness is abrupt and the patient experiences severe pain in the region

inflammatory reaction which may be acute or chronic

The etiology of bursitis is usually traumatic or infectious The bursæ placed in relation to pressure bearing areas the prepatellar bursa and the bursæ of the great toes are subjected to repeated trauma and often become the site of inflammatory swelling Elsewhere the subdeltoid bursæ may give rise to symptoms during the course of an upper respiratory infection or acute exacerbations of sinusitis, or in association with the presence of a periapical abscess

Special types of bursitis have been designated, depending upon the anatomic location and the probable etiologic factor *Subdeltoid bursitis* is recognized as a clinical entity The etiology is probably a combination of muscle strain trauma and infection Elevation of the arms for long periods of time promoting fatigue and injuries from falls may be sufficient to traumatize the tissue and permit chance infection In the early stages there is excruciating pain beneath the deltoid muscle and the patient is unable to elevate his arm There is localized point tenderness As the disease progresses adhesions form between the bursæ and its related tendons Finally the shoulder joint becomes fixed When this occurs a roentgenogram may show calcification within the bursæ Not infrequently the condition is bilateral

In the treatment of the first attack of acute subdeltoid bursitis some physicians recommend the application of heat particularly diathermy Injections of procaine hydrochloride (2 per cent solution) into the affected tissues often gives rise to immediate dramatic results In some cases the patient may enjoy permanent relief in other instances there may be a return of symptoms as the effect of the anesthetic agent wears off Relief of symptoms from the inflamed sac may result from needling the bursa under local anesthesia and aspiration of the fluid At times roentgen therapy gives prompt and continued relief In chronic cases surgical excision of the calcified bursa is the method of choice

Other frequent sites of painful inflammation are the olecranon bursa 'tennis elbow 'miner s elbow prepatellar bursa house maid s knee , and the bursa of the great toe, poor man s gout occasionally, the gluteal bursa, 'weaver s bottom

## THE VOLUNTARY MUSCLES

### Interstitial Myositis, Intramuscular Fibrositis

*Synonyms* —Primary intramuscular fibrositis, Muscular rheumatism —Interstitial myositis may be defined as a non suppurative swelling and fibroplastic proliferation of the muscle sheaths or fibers It is essentially a fibrositis but clinical types are recognized depending upon the tendinous insertions of the muscle involved

Lumbar Muscles (*Lumbago*) —The onset of symptoms of inflammation of fibrous tissues of the lumbar muscles is characterized by the sudden occurrence of pain and disability Upon questioning the patient carefully it is most always learned that some form of trauma or strain preceded the attack A sudden blow to the lumbar region may be a precipitating factor Strain incident to sudden lifting of a heavy object or elevating a stuck window,' may be sufficient to tear the fibrous attachments or sheaths of the lumbar muscles Symptoms arise quite frequently after assuming a stooping posture for a prolonged period of time Frequent examples of this are seen in individuals accustomed to sedentary habits becoming engaged in home gardening

The pain may be slight but it usually is agonizing in intensity The patient finds little comfort in any position Examination of the lumbar region reveals slight elevation of the skin due to hypertrophy of the muscles Spasm is detected by the palpating fingers The muscles are hard firm and contracted The muscle tension may cause curvature of the spinal column with concavity toward the affected side Constitutional symptoms usually are absent

*Differential Diagnosis* —The symptoms indicative of perinephric abscess may simulate lumbago Generalized symtomatology fever leukocytosis and signs of toxicity are present and aid in the differential diagnosis In renal calculus colicky pain usually radiates into the groin with accompanying urinary frequency and hematuria *Rupture*

infections of the muscles that show a tendency to suppurate They may be considered primary when a locus of infection results from some local trauma or penetrating wound to the tissues The bacterial agent is usually Staphylococcus aureus

Secondary suppurative myositis is an accompaniment of infections elsewhere in the body either by direct extension or metastasis Typhoid and meningococcic abscesses chronically draining sinuses due to coccidioides and the tubercle bacillus are examples

TRICHINOSIS —The clinical manifestations of trichinosis are described elsewhere in this book After gaining entrance to the blood stream the larvae of Trichinella spiralis invade the muscle tissues The diaphragm as well as many voluntary muscles is the site of invasion During this period of dissemination there is a local inflammatory reaction as the larvae become lodged in the muscle fibers The symptoms are largely muscle soreness pain and tenderness due to edema and swelling Later the wall of the cyst becomes calcified Treatment is entirely symptomatic

## NON-SUPPURATIVE MYOSITIS

DERMATOMYOSITIS (PRIMARY POLYMYOSITIS) —Dermatomyositis is a non suppurative inflammation of the skin subcutaneous tissues and muscles The disease once recognized by the clinician will be found to be less rare than usually is supposed

*Etiology* —The cause of dermatomyositis is unknown It may appear in persons who may have been thought to be in good health and who were living under good environmental circumstances It has occurred in athletes while in training and in fine physical form On the other hand O Leary and Waisman stated that infection or other disease preceded the onset of illness in the 40 cases studied by them

*Pathology* —There is a generalized thickening of the integument Areas of hyper keratosis are seen among which may be recognized small foci of epithelial necrosis There are edema and lymphocytic infiltration of the subcutaneous tissue An inflammatory reaction is present in the subjacent muscle consisting of areas of infiltration with lymphocytes The cellular infiltrate however, may be small even with severe myositis The changes in the muscles consist of dissolution and vacuolation of striated muscle shrinking of muscle substance and loss of striation In later stages there is caking of collagenous fibers which become swollen and highly refractile and break up into shreads and bars finally fusing into a homogenous mass

*Symptoms* —The onset of illness is insidious The patient at first complains of lassitude which later progresses to weakness and general debility There is a feeling of tenseness of the skin and the facial expression becomes more or less fixed There may be edema of the eyelids The muscles of the extremities are painful on motion and sore to the touch The skin in the affected areas feels thickened and indurated The disease process gradually extends over the entire body

The spleen and liver sometimes become palpable Slight enlargement of the superficial lymph nodes has been observed Sweating slight leukocytosis and a slight remittent fever usually are present The reflex reactions usually are reduced and sensory changes sometimes appear A transient arthralgia may accompany the illness and in severe cases contracture of the joints may result

The course of illness at times is acute but usually is subacute or chronic extending over a period of many months or years Death may result in severe cases

*Diagnosis* —The diagnosis of dermatomyositis may be established on finding the characteristic histologic pattern following biopsy of tissue The condition is to be differentiated from disseminated lupus erythematosus chronic eczema, erythema nodosum periarthritis nodosum and diffuse scleroderma

*Treatment* —The treatment is symptomatic

ACTH and cortisone have been used recently in dermatomyositis These agents are capable of altering the acute inflammatory and destructive process in the muscles however permanent remission from these agents alone is considered unlikely Thorn

of the diaphragm. The pain is accentuated by deep breathing and coughing. Fever, sweating and leukocytosis accompany the illness. The patient may experience three or four paroxysms of pain over a period of *from two to four days*. The treatment is entirely symptomatic. Uneventful recovery usually occurs.

INTERCOSTAL MUSCLES (*Pleurodynia, Intercostal Myalgia*).—A relatively common form of fibrositis is found in connection with the intercostal muscles. The symptoms are characterized by pain in the region of the lower intercostal muscles frequently adjacent to the attachment of the diaphragm. The serratus magnus and the pectoral muscles may be involved. The pain is aggravated by coughing, sneezing or full inhalation. There is hyperesthesia and deep tenderness in the intercostal spaces of the involved muscle. Spasm of the muscle may be felt.

Differential diagnosis must be made from acute pleurisy. This is an infectious process characterized by fever and general signs of toxemia. On auscultation a friction rub may be heard in the involved area during respiration. In the early stages of development of herpes zoster it may be difficult to establish the diagnosis. This is usually accompanied by an eruption of vesicles and fever. In intercostal neuralgia tender points may be determined with deep pressure on the nerve trunk along its course subjacent to the corresponding rib.

## MYOSITIS OSSIFICANS

TRAUMATIC MYOSITIS (*Traumatic Myositis Fibrosa*).—Injury to muscle bundles frequently results in tissue necrosis and hemorrhage. An example of this is the popularly known "Charlie horse" of the football player. There is a sudden rupture of muscle fibers and capillaries accompanied by hemorrhage in the tissues. In some cases there may be failure of complete resolution of the process and healing may consist in the formation of fibrous tissue and its resultant organization. Such lesions tend to undergo calcification. The reason for this deposition of calcium salts is obscure. It actually may progress to the formation of bone containing islands of blood formation.

MYOSITIS OSSIFICANS CIRCUMSCRIPTA (*Calcinosis Circumscripta*).—This name is given to a condition characterized by small areas of calcification scattered throughout the skin and subcutaneous tissues.

MYOSITIS OSSIFICANS PROGRESSIVA (*Calcinosis Universalis*).—This disease is of unknown etiology. The calcium and phosphorus levels of the blood are normal. The onset may occur early in life. There is a generalized calcification in the skin, interstitial tissues, tendons, fascia and muscles. At first the abnormality appears in a few localized areas as a fibrous tissue proliferation which spreads slowly over a period of time. The fibrous masses become indurated and undergo pathologic calcification. By extension of the process, fusion of various structures by fibrosis and bony growth occurs. The ligaments and joints become immobilized. True bone formation may extend through muscle, ligament and periosteum. Muscle atrophy becomes extreme. There may be a minimal amount of pain. Accompanying this is a slowly progressive fixation of the joints of the extremities and spine. Breathing may be restricted by fixation of the ribs and ossification of the muscles of respiration. Thus the unfortunate victim of this rare malady reaches a stage of total disability. The "ossified man" of the circus is an example of this condition.

Maldevelopment of the fingers and toes (microdactylia) has been reported as a frequent accompaniment and is thought to be congenital fault.

*Treatment*.—The treatment of traumatic myositis ossificans is preventive in character. Following trauma the injured tissues should be given immediate rest. Cold compresses should be applied and the muscles bound in a compression bandage in an attempt to prevent further hemorrhage. Later radiant heat directed to the area of injury may aid in absorbing the hematoma.

When ossification occurs, local excision of the foreign tissue by surgical procedure may be indicated. Treatment of myositis ossificans progressiva is unsatisfactory.

## PARENCHYMATOUS MYOSITIS

SUPPURATIVE MYOSITIS.—This terminology is used to designate a group of

contracted pelvis The combination of these causes the subject to assume a waddling gait

Achondroplastic dwarfs are physically active and mentally alert The sexual characteristics are normal. Sexual development may even be precocious

Until recently this condition was confused with cretinism. The cretin dwarf however is inactive physically and retarded mentally

HEREDITARY DEFORMING CHONDRODYSPLASIA (*Multiple Cartilaginous Exostoses*) —This is a rare disease in which there are many cartilaginous projections and bony exostoses appearing at the diaphyses of the long bones They have their origin from the primitive connective tissue which may differentiate into either bone or cartilage The disturbance results from abnormal stresses and strain interfering with the mechanical function of the joints The disease is not progressive after puberty and is more common in males than in females There are indications that heredity is a factor in its production If local symptoms are troublesome or deformity extreme the exostoses causing trouble may be removed surgically Some of these exostoses may be the seat of malignant change

OXYCEPHALY (*Steeple Head*) —A congenital defect with premature union of cranial sutures limiting growth of the skull except in the upward direction resulting in a tall pointed skull with marked exophthalmos Cranial nerve disturbance results from pressure and optic atrophy is apt to occur

LEONTIASIS OSSEA (*Hyperostosis of the Skull*) —A symmetrical enlargement of the bones of the skull and the mandible There is an irregularly distributed increase in density of the bone and a tendency to closure of the foramina with consequent damage of nerves and blood vessels The external measurements of the skull are greatly increased but the cranial cavity is encroached upon The skull may attain a thickness of 5 cm Pressure on nerves and brain cause the symptoms of headache paralysis blindness and convulsions

This rare disease becomes apparent most often during adolescence The course is chronic and may be interrupted by remissions As to diagnosis this condition is distinctive The etiology is obscure and treatment only palliative

HYPEROSTOSIS FRONTALIS INTERNA —This is the most distinctive of a group of calvarial changes Moore termed them metabolic craniopathies In this condition newly formed cancellous bone is deposited on the inner table of the frontal bone This bony mass may be nodular or uniform in outline Neither growth nor regression has been observed during periods of study Moore found 96 examples among the roentgen-ray plates of 6 650 persons examined and 135 cases showing other types of hyperostosis of the skull Nearly all of these reported cases occurred in women The symptoms include headache obesity of the pituitary type neuralgia of the fifth nerve hemiparesis and general weakness There may be an overgrowth of hair on the chin The symptoms are indefinite but may be severe and distressing Brain tumor often is suspected in these cases

HYPERTELORISM —Hypertelorism is a developmental congenital anomaly of the lesser wings of the sphenoid bones It is of rare occurrence Greig established the identity of this condition in 1924 when he described the complete clinical and pathologic findings in the cases he studied It was he who introduced the descriptive term hypertelorism Riley, in 1933 reported the data on four patients bringing the total number of cases to appear in the literature to 13

Hypertelorism may be recognized at birth because of the peculiar facies Due to the increased growth of the wings of the sphenoid bones the eyes are widely separated and the horizontal axis of the eyes is directed in a more lateral direction than is normal Mental deficiency usually accompanies this abnormality There is a familiar tendency to the anomalies of the sphenoid bone

LAURENCE-MOON-BIEDL SYNDROME —The Laurence-Moon-Biedl syndrome is of uncommon occurrence Riley and Lisser in their report state that 77 cases have been accumulated in the literature This syndrome according to these authors is characterized by dystrophia adiposo-genitalis atypical retinitis pigmentosa mental deficiency familial occurrence and skeletal abnormal-

and his associates have found that, once the initial improvement has been obtained with ACTH and cortisone testosterone due to its anabolic effect, may be useful in restoring the muscles as functioning units

BOECK'S SARCOID —Boeck's sarcoid is a disorder characterized by the formation of areas of induration and nodules in the skin and subcutaneous tissues At times there may be some associated changes in the bones and lungs (For further discussion *see* Chapter 10)

### REFERENCES

*Diseases of the Fibrous Tissues and Muscles*


BATTEN F E A Case of Myositis Fibrosa with Pathologic Examination Trans Clin Soc London 1904 37 226

BROCK W G Dermatomyositis and Diffuse Scleroderma Differential Diagnosis and Reports of Cases Arch Dermat and Syph, 1934 *30* 227

CODMAN E A The Shoulder Rupture of the Supra pinatus Tendon and Other Lesions In or About the Subacromial Bursa Boston, Thomas Todd Company 1934

LLEWELLYN, R L J and JONES A B Fibrositis London Rebman Company 1916

SCHMITTER F Sciatica and Fibrositis Historical and Recent Cults Theories and Facts as to Etiology Diagnosis and Treatment Indust Med 1938 7 82

SLOCUMB C H Differential Diagnosis of Periarticular Fibrositis and Arthritis Jour Lab and Clin Med 1936 *22* 56

THORN G W et al The Clinical usefulness of ACTH and Cortisone N E Jour of Med *242* 824-834 1950


## DISEASES OF THE BONES

SECONDARY HYPERTROPHIC PULMONARY OSTEO ARTHROPATHY (*Marie's Disease Hippocratic Fingers*) —*Secondary hypertrophic* pulmonary osteo arthropathy is a bulbous enlargement of the terminal phalanges of the fingers and toes In mild cases the swelling is commonly spoken of as clubbing of the fingers or designated as *Hippocratic fingers* Marie's syndrome is the term applied when the swelling is well advanced and there are associated changes in the larger bones of the extremities

This unusual swelling of the *terminal* phalanges is found commonly associated with bronchiectasis, congenital heart disease primary and secondary pulmonary neoplasms *mediastinal tumors* cor pulmonale abscess of the lungs and empyema In the author's experience the most marked enlargement of the fingers and toes was observed in a patient with extensive metastatic foci of carcinomatous tissue in the lungs

In mild cases the earliest signs noted may be *curvature of the nails as to both length* and breadth, parrot's beak The soft tissues gradually swell In cases which are well developed the terminal digits appear bulbous At times deposits of calcium beneath the periosteum of the fingers may be seen in the roentgenograms

The swelling is *unaccompanied* by pain or other symptoms There is no adequate explanation for the development of this swelling in the soft tissue of the terminal phalanges

### DEVELOPMENTAL DEFECTS AND MALFORMATIONS

ACHONDROPLASIA (*Chrondrodystrophia Fe talis*) —This is a dystrophy arising from premature union of the epiphyses with the diaphyses *Growth of the long bones is* inhibited and dwarfism results

*Etiology* —Heredity apparently is a factor in the production of this disorder Snoke reports an achondroplastic father and daughter the mother being normal He also reported transmission of achondroplasia in succeeding generations of families In one series 6 achondroplastic persons were found in 5 generations

*Clinical Characteristics* —Achondroplasia is a common cause of dwarfism Subjects *of this disorder are readily recognized* The person attains a height of from 3 to 4 feet The legs and arms are extremely short—disproportionately so in comparison with the torso There is an increase in the size of the *cranial vault and the basilar portion* of the skull is shortened Due to the abnormality of the cranial bones the face has a characteristic appearance The face seems abnormally broadened and flattened and the bridge of the nose is sunken The fingers are short and tridentate (trident hand) The posture is altered by lordosis and a

contracted pelvis The combination of these causes the subject to assume a waddling gait

Achondroplastic dwarfs are physically active and mentally alert The sexual characteristics are normal Sexual development may even be precocious

Until recently this condition was confused with cretinism The cretin dwarf, however is inactive physically and retarded mentally

HEREDITARY DEFORMING CHONDRODYSPLASIA (*Multiple Cartilaginous Exostoses*) —This is a rare disease in which there are many cartilaginous projections and bony exostoses appearing at the diaphyses of the long bones They have their origin from the primitive connective tissue which may differentiate into either bone or cartilage The disturbance results from abnormal stresses and strain interfering with the mechanical function of the joints The disease is not progressive after puberty and is more common in males than in females There are indications that heredity is a factor in its production If local symptoms are troublesome or deformity extreme the exostoses causing trouble may be removed surgically Some of these exostoses may be the seat of malignant change

OXYCEPHALY (*Steeple Head*) —A congenital defect with premature union of cranial sutures limiting growth of the skull except in the upward direction resulting in a tall pointed skull with marked exophthalmos Cranial nerve disturbance results from pressure and optic atrophy is apt to occur

LEONTIASIS OSSEA (*Hyperostosis of the Skull*) —A symmetrical enlargement of the bones of the skull and the mandible There is an irregularly distributed increase in density of the bone and a tendency to closure of the foramina with consequent damage of nerves and blood vessels The external measurements of the skull are greatly increased but the cranial cavity is encroached upon The skull may attain a thickness of 5 cm Pressure on nerves and brain cause the symptoms of headache paralysis blindness and convulsions

This rare disease becomes apparent most often during adolescence The course is chronic and may be interrupted by remissions As to diagnosis this condition is distinctive The etiology is obscure and treatment only palliative

HYPEROSTOSIS FRONTALIS INTERNA —This is the most distinctive of a group of calvarial changes Moore termed them metabolic craniopathies In this condition newly formed cancellous bone is deposited on the inner table of the frontal bone This bony mass may be nodular or uniform in outline Neither growth nor regression has been observed during periods of study Moore found 96 examples among the roentgen ray plates of 6 650 persons examined and 133 cases showing other types of hyperostosis of the skull Nearly all of these reported cases occurred in women The symptoms include headache obesity of the pituitary type neuralgia of the fifth nerve, hemiparesis and general weakness There may be an overgrowth of hair on the chin The symptoms are indefinite but may be severe and distressing Brain tumor often is suspected in these cases

HYPERTELORISM —Hypertelorism is a developmental congenital anomaly of the lesser wings of the sphenoid bones It is of rare occurrence Greig established the identity of this condition in 1924 when he described the complete clinical and pathologic findings in the cases he studied It was he who introduced the descriptive term hypertelorism Riley in 1933 reported the data on four patients bringing the total number of cases to appear in the literature to 13

Hypertelorism may be recognized at birth because of the peculiar facies Due to the increased growth of the wings of the sphenoid bones the eyes are widely separated and the horizontal axis of the eyes is directed in a more lateral direction than is normal Mental deficiency usually accompanies this abnormality There is a familiar tendency to the anomaly of the sphenoid bone

LAURENCE MOON BIEDL SYNDROME —The Laurence Moon Biedl syndrome is of uncommon occurrence Riley and Lisser in their report state that 77 cases have been accumulated in the literature This syndrome according to these authors is characterized by dystrophia adiposo-genitalis atypical retinitis pigmentosa mental deficiency familial occurrence and skeletal abnormal



FIG 223 —Paget s disease



FIG 224 —Paget s disease Sarcomatous degeneration with metastases in the lungs

ities The outstanding defect in development of the bones is a tendency to polydactylism

Some improvement has been reported following the administration of thyroid extract

PAGET'S DISEASE (*Osteitis Deformans*) — This is a chronic disease of the skeleton and is characterized by thickening and softening of the bones There are marked skeletal deformities shortening of the stature enlargement of the head and a tendency to pathologic fractures There may be an associated sarcomatous degeneration

*Etiology* —This condition first was described by Sir James Paget in 1877 It has become well recognized as a clinical syndrome The etiology is unknown

*Pathology* —The structural changes in Paget's disease first make their appearance in the skull tibiæ pelvis vertebræ and later the femora and humeri Circumscribed areas of decalcification appear and the involved areas become softened Interspersed irregularly between these areas the bone still retains calcium but it may appear more porous than normal There is an increase in vascularity of the tissue

The altered metabolism in the calcium chemistry of the bone results in thickening of the cortex but the structure has less tensile strength than normal In the skull the most marked changes are in the outer plate and diphlœ resulting in an immense thickening The circumference of the skull becomes greatly increased The cortex of the tibiæ becomes thickened and undergoes changes in shape The tibiæ tend to bow anteriorly and laterally The pelvis becomes broadened the femora become bent and eventually show a forward convexity With the absorption of calcium from the bodies of the thoracic vertebræ weakness ensues and collapse subsequently takes place The spine therefore assumes marked kyphosis

The pathologic changes may be complicated by the appearance of areas of sarcomatous degeneration in the bones Metastases from such areas may appear in the lungs or elsewhere in the body

*Symptoms and Course of Illness* —The onset of illness is insidious and the course a slowly progressive one Pain may be the first symptom Primarily dull and aching in character it increases in intensity with the passage of time The patients describe it as a deep constant dull aching pain Some patients however may go along for years experiencing only a minimal amount of pain

Information concerning the time of onset of the disease may be gained from inquiring into the patient's experience in buying hats It may be learned that years prior to the onset of pain or disability the patient found it necessary to buy new hats at frequent intervals because of the increasing circumference of the skull

There is a progressive kyphosis of the spine leading to marked shortening in stature As much as 10 inches in loss of height may be noted in a patient when standing

The shortened stature pendulous abdomen, large protruding head bowed shin bones and waddling gait combine to give the patient the characteristic habitus of advanced Paget's disease

The increased porosity of the bones renders them susceptible to fracture from slight trauma Tripping on the stairs or other forms of sudden contraction of the hamstring muscles against their apponens may be sufficient to cause a break of the femur Due to kyphosis fracture of the sternum is not unusual

*Diagnosis* —The roentgen ray examination reveals the osseous changes characteristic of Paget's disease In the early stages small circumscribed areas of irregularly scattered bony absorption may be seen in larger areas of density As the process of osteoporosis and intervening osteosclerosis advances shadows of increased density appear in the roentgenograms comparable to 'tufts of cotton These early changes not infrequently are observed in the roentgen films without the presence of the condition having been suspected clinically

In advanced cases the thickening of the bones become apparent The shadows cast by the trabeculæ become course and prominent In some areas the caliber of the marrow cavity may be encroached upon and narrowed elsewhere there may be widening

The roentgenograms offer little difficulty in differential diagnosis from conditions

in which the bony changes are essentially osteogenic in character As a rule it is easily distinguished from carcinomatous metastasis, multiple myeloma and osteitis fibrosa cystica

Blood chemistry determinations may be of aid in diagnosis The calcium and phosphorus levels will be within normal values but the serum alkaline phosphatase will be high

In patients with Paget s disease seen on our wards at the University of California Hospital, we have been impressed by the high incidence of nodular goiters The majority of these patients show an increased intestinal absorption of carbohydrates such as is seen in patients with goiter They also show a "low carbohydrate tolerance which is, in fact, an alimentary glycosuria In such instances the clinical picture resembles that of mild diabetes

*Treatment* —Patients suffering from pain will require analgesics Roentgen ray irradiation over painful areas may afford some relief The administration of ascorbic acid daily in amounts up to 1 gm may ease the bone pain There are no satisfactory means of treating the fundamental condition

Osteitis Fibrosa Cystica Generalisata —*In this condition multiple areas* of absorption appear in the bones followed by fibrous tissue replacement and cyst formation Fracture or bending of the long bones is of frequent occurrence For a clinical description of this condition and discussion on physiological chemistry the reader is referred to Chapter 16

Osteomalacia —This condition is characterized by a tendency to repeated fractures resulting from decalcification and increased brittleness of the bones Control studies to determine the excretion of calcium carried out according to the plan outlined by Aub show a marked increase in the excretion of this chemical, presumably it is removed from the bones Although there is evidence to show that the output is increased the blood calcium level remains at a normal value Content of phosphorus in the blood may be slightly reduced and the phosphatase activity slightly increased

The *etiology* of this condition is obscure The disease has been reported to appear most frequently in women Repeated pregnancy at frequent intervals may be a *predisposing factor* wherein the balance between deposition of calcium in the fetal bones and the bones of the mother is disproportionate Lack of vitamin D may play a role in the development of some of these cases and in this respect simulates rickets

The onset of illness is insidious Fracture may result from trivial trauma or over exertion of one muscle group against another *Roentgenograms will show the marked* porosity and rarefaction of the bones

The course of illness is chronic Some strengthening of the bones may result from intensive therapy with calcium vitamin D or cod liver oil concentrates

A word of caution is to be offered in connection with overdosage with vitamin D concentrates An elderly physician seen by us had a high calcium and magnesium *content in the kidneys and muscles through*out the body from the daily ingestion of large amounts of a preparation of vitamin D concentrate Death resulted from uremia

## Idiopathic Fragility of Bones

Hereditary Type of Hypoplasia of the Mesenchyme (*Brittle Bones and Blue Sclera*) —This condition is rare but large family groups have been traced Hill and McLanahan report characteristic signs in 27 of 51 members of five generations in a family studied by them Burch and Sodeman found 41 persons affected of 76 observed in a study of members of five generations in still another family

This seems to be a distinct clinical entity attributed to a hypoplasia of the mesenchyme transmitted as a dominant characteristic according to the Mendelian law Those affected are usually slender the scleræ show a bluish color attributed to thinness of the membrane Otosclerosis with deafness develops at an early age in a large proportion of these subjects Fractures occur throughout childhood but are not frequent after puberty Healing of fractures is not delayed and there is no undue deformity

This condition may cause little trouble in adult life No form of treatment is known

to be of value. There are reports of apparent favorable reaction from strontium lactate and calcium phosphate. Cod liver oil concentrates are recommended.

CONGENITAL TYPE (*Osteopsathyrosis; Osteogenesis Imperfecta; Lobstein's Disease; Fragilitas Ossium*).—A congenital defect of bone formation in which the bones are delicate and fragile, the cortex thin and the marrow cavity enlarged. Fractures of the bones occur on slight strain or injury. Lewin mentions a teacher aged fifty years who has had one hundred and twelve fractures and is still active in her work. This form of fragility is not shown to be hereditary; it occurs as the strictly congenital type with the bone defects developed in fetal life with death usually taking place in infancy. Or it may be due to osteogenesis imperfecta tarda wherein the appearance of symptoms is delayed. As a result calcium metabolism is disturbed. Cod liver oil, calcium and phosphorus are recommended.

SENILE OSTEOPOROSIS.—This is a systemic loss of calcium from the skeletal system. It occurs along with the physiologic and metabolic changes that characterize the aging process. Normally there is a daily breakdown and repair of osseous tissue by the osteoclasts and osteoblasts. In the aged, osteoblastic activity is lessened with a resultant failure to deposit calcium in the organic matrix. This results in a decreased calcium content of the bones.

The systemic calcification is accompanied by brittleness and softening of the bones. The bodies of the thoracic vertebra become compressed and the spine bowed, hence the kyphotic spine of age atrophy. Fracture of the bones occurs frequently. The head, neck, and shaft of the femur and the pelvic bones are most frequently the sites of pathologic fracture.

The diagnosis of senile osteoporosis usually can be established from the radiograms. The decalcification is widespread throughout the skeletal system.

The etiology of osteoporosis is not definitely known. Albright is of the opinion that the disturbance is a failure of the osteoblasts to lay down bone matrix. He discusses three factors which might influence osteoblastic activity: (*a*) steroidal hormones; (*b*) mechanical stresses and strains; (*c*) nitrogenous building blocks. The osteoporosis of old age is partly attributed to the loss of gonadal hormones and adrenal-cortical N hormone and may respond to appropriate estrogen and testosterone therapy.

It is well known that mechanical stresses and strains stimulate osteoblastic activity and the sedentary habits of the aged individual may lead to osteoporosis through atrophy of disuse.

The production of bone matrix is undoubtedly influenced by the availability of certain nitrogenous substances such as the serum albumin. In such conditions as starvation, malnutrition, and nephrosis, conditions in which the serum albumin is low, osteoporosis is common.

## CONDITIONS CHARACTERIZED BY SCLEROSIS OF THE BONES

Two types of osteosclerosis are recognized: the so-called marble bone or Albers-Schonberg disease, and myelosclerosis or myelofibrosis.

MARBLE BONES (*Albers-Schonberg Disease; Osteosclerosis Fragilis Generalisata; Osteopetrosis*).—In osteosclerosis the essential lesion is one primarily of excessive bone formation. There is gradual thickening of the cortex and encroachment on the medullary cavity. The condition occurs usually in childhood and persists throughout life into adulthood. All of the bones of the body including the vertebrae and the skull may be affected. Due to increased calcification the bones become extremely dense and of marble-like texture. When attempting biopsy of such tissues the surgeon encounters extreme resistance of the tissue against the bite of the rongeur.

Unmistakable pictures which are characterized by the dense sclerosing process are revealed in the roentgenograms.

As the thickening of the cortex progresses the medullary cavity is encroached upon and the illness may terminate with a myelophthisic type of anemia.

The etiology of this comparatively rare condition is unknown.

MYELOFIBROSIS (*Fibrosis of the Bone-marrow—Myelosclerosis*) —This type of sclerosing process usually appears after the second decade The onset of illness is insidious and may be characterized by deep bone pain or tenderness The patient may consult his physician because of some symptom referable to an abnormality in hematopoiesis Mettier and Rusk reviewed the literature and reported two cases The clinical course may be typically that of true leukemia, or the patient may have a leukemoid blood picture characterized by leukopenia and a hemorrhagic tendency Enlargement of the spleen may be found on physical examination

Examination of tissue removed from the marrow cavity reveals the presence of fibroblastic proliferation A few spicules of cancellous bone may be present The hemopoietic tissue is disrupted and in many areas is obliterated

MELORHEOSTOSIS —This is a rare abnormality of the bones The condition was first described by Leri and Joanny in 1922 The structural changes are represented by hyperostosis of the cortex of the bones There is excessive formation of a dense sclerotic bone which may be of endosteal or periosteal origin The changes are usually unilateral in distribution and affect the long bones Thirty-nine such cases have been reported in the literature Recently, Carpender and his associates reported two additional cases but claimed distinction in that one case showed a bilateral distribution

Attention may be attracted to the presence of such a lesion by localized soft tissue swelling or tenderness A patient recently examined by us complained of localized tenderness and swelling just above the knee which she believed was sustained from a slight blow There was localized swelling and deep tenderness without evidence of redness or bruising The roentgenograms revealed the changes characteristic of melorheostosis This is characterized by the sclerosis of the bones giving an appearance of flowing or dripping suggestive of the dripping of candle wax Roentgenograms of this condition once seen will leave a vivid impression



FIG 225 —Melorheo tosis

Blood chemistry reveals normal values for calcium phosphorus and phosphatase levels The etiology is unknown

MISCELLANEOUS DISEASES OF THE BONES

SPONDYLOLISTHESIS.—Spondylolisthesis is the term applied to the symptom complex resulting from forward subluxation of the fifth lumbar vertebra. This abnormality may result from some congenital anomaly or may be precipitated by trauma. Elongated transverse processes of the fifth lumbar vertebra may be an accompaniment. Pain is the outstanding symptom and may be described by the patient as a dull aching sensation low in the back. It may be relieved by rest. In cases of long-standing illness there is pain along the distribution of the sciatic nerve. Stiffness supervenes and restriction of forward bending frequently results. Marked lordosis may be present.



FIG. 226.—Spondylolisthesis.

The diagnosis is established on examining the roentgenogram. The lateral view may reveal the subluxation to best advantage.

SPINA BIFIDA.—This is a congenital anomaly due to failure of the neural arch to close. This varies in degree from a slight linear defect discernible in the roentgen film to a wide gape in the fifth lumbar and upper sacral vertebræ. When wide open there may be a sac like protrusion of the meninges (meningocele) that is rather serious in nature.

NEOPLASTIC DISEASES OF THE BONES

The sudden appearance of pain or swelling in the region of a bone not infrequently is the first sign of neoplastic degeneration. Benign and primary tumors usually can be diagnosed from the roentgenogram. Metastatic malignancies require careful clinical investigation in order to determine the primary source.

The classification of tumors of the bones recommended by the Bone Tumor Registry of the American College of Surgeons is shown in Table 65.

BONE CYST.—This is a solitary lesion which appears most frequently near the

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FIG 225 —Melorheostosis

Blood chemistry reveals normal values for calcium phosphorus and phosphatase levels The etiology is unknown

### Miscellaneous Diseases of the Bones

Spondylolisthesis.—Spondylolisthesis is the term applied to the symptom complex resulting from forward subluxation of the fifth lumbar vertebra. This abnormality may result from some congenital anomaly or may be precipitated by trauma. Elongated transverse processes of the fifth lumbar vertebra may be an accompaniment. Pain is the outstanding symptom and may be described by the patient as a dull aching sensation low in the back. It may be relieved by rest. In cases of long standing illness there is pain along the distribution of the sciatic nerve. Stiffness supervenes and restriction of forward bending frequently results. Marked lordosis may be present.



Fig. 296.—Spondylolisthesis.

The diagnosis is established on examining the roentgenogram. The lateral view may reveal the subluxation to best advantage.

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### Neoplastic Diseases of the Bones

The sudden appearance of pain or swelling in the region of a bone not infrequently is the first sign of neoplastic degeneration. Benign and primary tumors usually can be diagnosed from the roentgenogram. Metastatic malignancies require careful clinical investigation in order to determine the primary source.

The classification of tumors of the bones recommended by the Bone Tumor Registry of the American College of Surgeons is shown in Table 65.

Bone Cyst.—This is a solitary lesion which appears most frequently near the

proximal end of the shaft of the long bones. It is usually found in persons under twenty years of age. The humerus is a frequent site for this formation which is found, incidentally, on roentgen ray examination of the skeleton. Pain or swelling is seldom present. Due to the expansion of the lesion there is pressure atrophy of the cortex of the bone, and as a result, pathologic fracture may occur.

The roentgenogram reveals the presence of a smooth, symmetrically expanded new growth within the medullary cavity. There

Trauma appears to be a precipitating factor. The lesion develops rapidly and a globular swelling can be felt; pain becomes the outstanding symptom. Geschickter and Copeland are of the opinion that the giant cell tumors are of subperiosteal origin. The osteoclasts proliferate as a result of an injury.

The roentgen manifestations are those of a solitary tumor mass that has expanded and caused pressure atrophy of adjacent bone. The mass appears somewhat translucent and trabeculated.

TABLE 65.—REVISED CLASSIFICATION OF BONE TUMORS (1939)

| | Malignant | Benign |
|---|---|---|
| I Osteogenic series—*osteogenic sarcoma* | 1 Medullary and subperiosteal | 1 Exostosis |
| | 2 Telangiectatic | 2 Osteoma |
| | 3 Sclerosing | |
| | 4 *Periosteal* | |
| | 5 Fibrosarcoma | |
| | (a) Medullary | |
| | (b) *Periosteal* | |
| | 6 Parosteal capsular | |
| II Chondroma series | 1 Chondrosarcoma | 1 Chondroma |
| | 2 Myxosarcoma | |
| III Giant cell tumor series | 1 Malignant | 1 Epiphyseal giant cell tumor |
| IV Angioma series | 1 *Angio-endothelioma* | 1 *Cavernous angioma* |
| | 2 Diffuse endothelioma | 2 Plexiform angioma |
| V Myeloma series | 1 Plasma cell | |
| | 2 Myelocytoma | |
| | 3 Erythroblastoma | |
| | 4 Lymphocytoma | |
| VI Reticulum cell lymphosarcoma | | |
| VII Liposarcoma | | |

is no evidence of penetration into the osseous tissue.

Treatment is usually surgical and not necessarily indicated unless pain is marked or spontaneous fracture occurs.

BENIGN GIANT CELL TUMOR.—Benign giant cell tumor of the bone is a solitary lesion. It usually appears after the second or third decade. The lesion is most frequently located just above or below the knee. It has been reported in the radius but is of less frequent occurrence in the bones of the skull. The lesions are usually in the long bones at or near the epiphyses where cartilage is undergoing osteogenesis.

The diagnosis can be established on biopsy of the tumor. The tissue appears hemorrhagic and is friable. The histologic findings consist of the presence of large numbers of multinucleated giant cells without much evidence of fibroplastic proliferation.

Benign giant cell tumors usually respond well to treatment with roentgen ray irradiation.

Benign giant-cell tumor is to be distinguished from eosinophilic granuloma of bone (See Chapter 26).

OSTEOLYTIC SARCOMA (*Sclerosing Type*).—This is a highly differentiated type of bone sarcoma. It is most often found in young persons between fifteen and twenty-

five years of age The tumor is made up of large numbers of osteoblasts The lesion is essentially a proliferative one and according to Geshickter and Copeland osteogenesis may arise from intracartilaginous or membrane tissue There is an admixture of osteoid tissue with actual spicules of bone fine spicules of bone Metastases of the tumor to the lungs may occur by the bloodstream

In the roentgenograms the abnormal tissue appears as dense, irregular areas of newly formed bone radiating from within the shaft of the bone out into the soft tissue



FIG 227—Giant cell tumor of the lower end of the femur in a young girl aged twenty two years (Comroe s Arthritis)

There is local extension of the process through the cortex of the bone and into the regional soft tissues On clinical examination soft tissue swelling is usually *apparent and there* may or may not be tenderness on pressure Crepitus may be felt on palpation due to the presence of

The treatment consists of amputation of the affected limb if there is no clinical evidence of metastases

OSTEOLYTIC SARCOMA (*Osteolytic Form*) — Clinically this type of sarcoma is differentiated from the sclerosing type with considerable difficulty It is a highly *de*

proximal end of the shaft of the long bones It is usually found in persons under twenty years of age The humerus is a frequent site for this formation which is found incidentally, on roentgen ray examination of the skeleton Pain or swelling is seldom present Due to the expansion of the lesion there is pressure atrophy of the cortex of the bone, and as a result, pathologic fracture may occur

The roentgenogram reveals the presence of a smooth symmetrically expanded new growth within the medullary cavity There is no evidence of penetration into the osseous tissue

Treatment is usually surgical and not necessarily indicated unless pain is marked or spontaneous fracture occurs

Benign Giant Cell Tumor —Benign giant cell tumor of the bone is a solitary lesion It usually appears after the second or third decade The lesion is most frequently located just above or below the knee It has been reported in the radius but is of less frequent occurrence in the bones of the skull The lesions are usually in the long bones at or near the epiphyses where cartilage is undergoing osteogenesis

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| | 6 Parosteal capsular | |
| II Chondroma series | 1 Chondrosarcoma | 1 Chondroma |
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| III Giant cell tumor series | 1 Malignant | 1 Epiphyseal giant cell tumor |
| IV Angioma series | 1 Angio-endothelioma | 1 Cavernous angioma |
| | 2 Diffuse endothelioma | 2 Plexiform angioma |
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| | 2 Myelocytoma | |
| | 3 Erythroblastoma | |
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| VII Liposarcoma | | |

The diagnosis can be established on biopsy of the tumor The tissue appears hemorrhagic and is friable The histologic findings consist of the presence of large numbers of multinucleated giant cells without much evidence of fibroplastic proliferation

Benign giant cell tumors usually respond well to treatment with roentgen ray irradiation

Benign giant-cell tumor is to be distinguished from eosinophilic granuloma of bone (See Chapter 26)

Osteolytic Sarcoma (*Sclerosing Type*) — This is a highly differentiated type of bone sarcoma It is most often found in young persons between fifteen and twenty

and lymph nodes. A fatal termination of the illness usually occurs after a period of a few months to one or two years.

MULTIPLE MYELOMA (*Plasmacytoma, Plasma Cell Myeloma*).—This highly malignant disease of the bones, in the experience of the writer from observing cases on the wards of the University of California Hospital, may be of more frequent occurrence than is generally supposed. As the name implies, multiple tumors are present throughout the skeletal system. (For further discussion of this disease *see* Chapter 25.)

METASTATIC MALIGNANCY.—Metastatic malignancies to the bone show certain characteristics in the roentgen films which permit recognition of two types of reaction. The one most frequently observed is osteolytic (bone destroying) in character and the other is osteoblastic (bone forming). The metastatic lesions stimulating osteolytic activity are recognized by decalcification and destruction of bone. In the osteoblastic metastases there is increased calcification and the tendency to new bone formation around carcinomatous processes.

Carcinoma of the breast, according to most authors, is one of the primary tumors that metastasizes most frequently to the bones. The medullary cavities or osseous tissue of the vertebrae, the pelvis, the femur and the skull are the regions likely to be invaded. In the roentgenograms the metastatic lesions are seen as irregularly outlined translucent areas of varying size. Some may be surrounded by merely a thin shell of bone. Such foci are usually multiple.

In most cases of bone metastasis a primary carcinoma of the breast has been recognized clinically and the phenomenon of dissemination occurs during the course of illness. In our experience, however, the clinical recognition of such metastases have occurred as late as eleven years after the removal of a breast for carcinomatous degeneration. On the other hand, a metastatic focus may be found in a patient who is entirely unaware of a tumor nodule in the breast.

Lesions of metastatic carcinoma of the bone that are essentially osteolytic in nature may come from primary sources other than the breast. Hypernephroma, carcinoma of the thyroid, bronchogenic carcinoma, neuroblastoma and carcinoma of the rectum not uncommonly disseminate through the blood stream to the bones.

Carcinoma metastases stimulating osteoblastic activity are limited almost entirely to those arising primarily from the prostate. In the roentgenograms these lesions are recognized by varying sized translucent foci surrounded by an increased density of the bone. The pelvis, vertebrae, upper end of the femur and the skull may show such lesions.

Clinically, pain is the most outstanding symptom which may call attention to a focus of carcinomatous metastasis. At first it may be dull, aching and intermittent in character, becoming constant and agonizing later. In contrast to this there may be an abrupt onset of excruciating pain accompanied by disability. A metastatic nodule may be suspected in the region of the pain if there is spasm of the regional muscles, slight pitting edema and deep bone tenderness.

It is not uncommon to find an altered blood picture during the course of illness. There is usually a normochromic or normocytic type of anemia. There may be a leukopenia or leukocytosis. Normoblasts and myelocytes may be observed in the blood films.

In patients with carcinoma of the breast metastasizing to the bones there may be slight elevation of the serum calcium, phosphorus and phosphatase levels. Gutman and Gutman have shown that the acid phosphatase level of the blood serum is definitely increased in metastatic cancer of the prostate to the bones. In the early reports it was believed that the amount of cancer metastasis could be correlated with the amount of acid phosphatase in the serum. Recent studies, however, are not entirely in agreement.

Roentgen ray irradiation of the bones has been the method of choice in the treatment of carcinomatous metastases. Relief of pain may come to some patients, whereas this method of treatment may only aggravate the symptoms of others. The method is only palliative.

In some of the recent experimental work it is suggested that estrogenic substances may play a role in the rate of growth of

structive growth extending through the shaft and cortex of the bone without much tendency to invade the surrounding tissues Due to the extension of the lesion within the bone and its resultant decalcification the tumors are soft and fluctuant There is increased vascularity within its structure—the vascular engorgement of which has been referred to as 'bone aneurysm The tissue on microscopic examination is found comprised of osteoblasts among which are many mitotic figures Intermingling within these or closely associated with them are large, malignant-appearing spindle cells

In the roentgenograms there is evidence of much destruction of bone Almost the entire circumference of the shaft of the bone may be replaced by a translucent new growth There may be some evidence of osteoblastic proliferation and the formation of spicules of bone but not to the extent that is characteristic of the sclerosing type of growth

Chondromas —Chondromas are localized overgrowths of cartilage that may appear in any region where there is cartilage Ewing states that there is a tendency for these structures to reproduce normal types of cartilage Ossification of these benign tumors may occur

Chondrosarcoma —Primary chondrosarcomata involving the bones is comparatively rare It is of a highly malignant nature, occurring at about the age of puberty

Ewing's Tumor (*Ewing's Sarcoma Ewing's Endothelial Myeloma Myelo-endothelioma*) —Ewing's sarcoma is a comparatively rare form of bone tumor appearing in the second and third decades of life Men more frequently are affected than women The etiology of this condition is obscure but trauma is thought to be a contributing factor The primary site may be the middle of the shafts of the long bones but metastases may go to the flat bones Pain is the outstanding symptom and may be more severe at night It is usually described as dull and aching in character with periods of remission and exacerbation Early in the course of illness a swelling is sometimes to be found on examination As the disease progresses a large fusiform swelling appears which may extend the entire length of the bone

There has been considerable difference of opinion concerning the origin of this tumor The cells comprising the tumor are small round cells which possibly arise from the lymphatic channels Ewing considers the tumor as non osteogenic in origin and classifies it as an endothelial myeloma



Fig 228 —Ewing's sarcoma in middle third of humerus

Pancoast states the bones present no characteristic roentgen appearance in Ewing's tumor The onion peel osteoblastic reaction often referred to may also be found in other lesions

The tumor cells are sensitive to the roentgen ray and following a course of treatment the swelling may subside Recurrences of the local lesion are prone to occur Metastases have been reported to the lungs skull

# PART VI
# CARE OF AGED AND REHABILITATION

## Chapter 29

# The Care of the Aged

By RICHARD A. KERN, M.D.

*Gerontology* is a study of all aspects of old age: the processes of aging, the retardation of those processes and the minimizing of their effects, the manifold problems that accompany old age, the ways in which those problems can best be solved.

*Geriatrics* deals only with the medical aspects of gerontology.

The importance of nonmedical factors in the causation of a disease and in the management of the person with that disease receives daily emphasis in medical practice. The physician knows, and the student must learn, that such matters as the social environment and the economic status of the patient must be considered in solving the medical problems of his patient. But in general the textbook of medicine gives scant notice to such nonmedical factors, chiefly because of limitations of space and partly because of their discussion in other texts.

An exception to this usage must be made in presenting this chapter on the care of the aged. There are several reasons why the nonmedical aspects of gerontology must here be stated in some detail. The problems posed by the aged in such fields as economics, politics, philosophy, religion and medicine have assumed formidable proportions only within the present generation. Moreover, they are increasing at a rate that will double their importance within decades as compared with centuries in the past. There are as yet no ready solutions for many of these problems, since they have become pressing only very recently and so have attracted little thought or attention heretofore. It is therefore the more important to state the problems in order to enlist new workers in their study.

*Increase in Average Longevity.*—The average length of life in Rome in Cicero's time was 23 years. In England about the year 1000 it was 35 years. (In India today it is still only 27 years.) In the United States in 1900 it was 47 years, an increase of only 24 years in nearly 2 thousand years. But in 1948 our figure stood at 67 years, and it will reach 70 in the early 1950's.

*Increase in Percentage of Aged in the Population.*—In 1850 only 2.6 per cent of the people of the United States had reached the age of 65. In 1950 those over 65 constitute about 8 per cent of the population and, according to the actuarians, will constitute 14.5 per cent by 1980. These are average figures; higher percentages obtain in certain areas (West Coast, New England) and in urban populations. The 1940 census listed as over age 65 some 8.2 per cent in San Francisco, 8.3 per cent in Los Angeles, 8.7 per cent in Oakland, 8.7 per cent in Seattle and 9.5 per cent in Portland, Oregon. The aged are forcing themselves on our attention by the sheer weight of their numbers.

The chief reasons for the longer average life are decreased infant mortality and the

cancer of the breast and prostate It has long been known that castration of a man with carcinoma of the prostate will inhibit the growth of metastatic foci in the bones Huggins recently reopened the subject and reported that following castration a considerable number of his patients remained symptom free for over thirty months Dean, Twombly and Woodward report the results of their work on chemical castration produced by the administration of stilbestrol The outcome closely parallels that of castration produced through surgical measures

In regard to carcinoma of the breast Taylor has shown that the injection of female hormone (estrogen) in mice of high cancer incidence will stimulate alteration of breast tissue Dresser has shown that temporary regression of extensive metastasizing cancer of the breast in women while still in the menstruating age may be induced by irradiation of the ovaries A great deal of interest has arisen regarding the favorable effects of testosterone on the course of mammary cancer Symptomatic relief and quiescence of osseous metastases have been reported in certain patients However the results have so far been unpredictable and transient The Therapeutic Trials Committee of the Council of Pharmacy and Chemistry of the American Medical Association is conducting an intensive investigation of this problem At present no definite conclusions can be drawn

## Chemical Poisons

**Fluorine Poisoning** —Absorption of fluorine is an industrial hazard encountered by workers in rock having a high fluorine content Fluorine poisoning may also result from the ingestion of sodium fluoride contained in roach powders Changes occur in the bones characterized by increased density and a tendency toward brittleness

**Radium Poisoning** —Radium poisoning has been an industrial hazard resulting from the ingestion of soluble radium salts over a long period of time The use of radium in the manufacture of luminous watch dials has been stopped through legal measures Precautionary measures against exposure to radioactive substances are being instituted in medical laboratories and industries where this material is used Cases of radium poisoning are therefore becoming of rare occurrence The bone changes consist of extensive areas of necrosis and absorption of osseous tissue There is a tendency toward pathologic fractures The course of illness may run a period of years The patient eventually succumbs to an aplastic type of anemia

## REFERENCES

### *Diseases of the Bones*

Albright F and Reifenstein E C Jr The Parathyroid Glands and Metabolic Bone Disease Baltimore Williams & Wilkins 1948 284

Bloodgood J C and Geschickter C F Tumors of Bones Cyclopedia of Medicine 1931 *2* 617

Burch G E and Sodeman W A Hereditary Hypoplasia of the Mesenchyme Am Jour Med Sci 1937 *194* 844

Carpender J W J Baker D R Perry S P and Outland T Melorheostosis Report of A Bilateral Case Am Jour Roentgenol and Radium Therapy 1943 *49* 398

Hills R G and McLanahan Samuel Brittle Bones and Blue Scleras in Five Generations Arch Int Med 1937 *59* 41

Mettier S R and Rusk G Y Fibrosis of the Bone Marrow (Myelofibrosis) Associated with a Leukemoid Blood Picture Am Jour Path 1937 *13* 377

Pepper O H P and Pendergrass F Hereditary Occurrence of Enlarged Parietal Foramina Am Jour Roentgenol 1936 *35* 1

Reilly W A Hypertelorism Jour Am Med Assn 1931 *96* 1929

Reilly W A and Lisser H Laurence-Moon Biedl Syndrome Endocrinology 1932 *16* 337

Schumacher I C Williams O O and Coltrin G S Plasma Cell Myeloma and Hyperproteinemia Calif and West Med 1937 *47* 1

*State old-age pensions* vary widely in amounts depending on the economic resources of the individual states. In 1948 such pensions ranged from a low of $18.79 a month in Mississippi to a high of $70.63 a month in California. Pennsylvania paid $40.12 a month. If these figures are compared with the basic cost of living per couple per month at that time—$125 to $152, depending on the state—it is clear that such old-age pensions fall short of providing even the barest subsistence in most instances. To the suggestion "why not higher pensions?" the obvious answer is: it would be very expensive. If all the aged were eligible for a $75 pension at age 63, the cost for the nation as of 1948 would have been 11.7 billions of dollars. Exactly that pension was voted in California in November 1948, but a year later, when the financial resources of that state seemed seriously threatened, the plan was modified by raising the pensionable age to 65. In 1949 California had 245,295 persons on old-age pensions, nearly 3 times as many as Pennsylvania with about the same total population.

State old-age pension plans, as well as social-security programs, are open to one important criticism: they are not based on sound actuarial principles. They are all on a "pay-as-you-go" basis, that is, benefits come out of current tax income rather than out of financial reserves. When times are good, tax income is high and potential beneficiaries are relatively few, the plans seem secure enough. But what will happen when times are less prosperous, tax income is lower or has been diverted to other more pressing expenditures, and potential beneficiaries have greatly increased?

4. *By Private Pension Plans.*—An increasingly important source of subsistence funds for the aged is developing in nongovernmental pension plans. Their rapid growth is evident from these figures: In 1941 only 600,000 persons in the United States had such coverage. By early 1949 their number had risen to 6,500,000, and the 9 million mark will have been reached during 1950. A significant fact is the adequacy of the pensions involved. Of those in force in 1949 only 25 per cent were for less than $100 a month, 55 per cent were for $100 to $125, and 20 per cent for over $125.

These private pension plans are of 2 chief types: *individual pension insurance* for premiums paid to an insurance company by the persons insured, and *industrial pension insurance*, in which the employer guarantees to the employee certain pension rights ("deferred wages"), often with payment participation by the employee out of wages, and variously administered as to cash reserves, re-insurance and supervision. Both types are on an actuarial basis.

But there are certain weaknesses in many industrial plans. In periods of depression not necessarily of a general nature but in a particular industry or in a given company (*e.g.*, when new inventions make an older product obsolete) there may be difficulty in meeting pension payments unless there are strong cash reserves. Yet it may be difficult to set up adequate cash reserves, especially at the time of installation of a pension plan. Only the strongest and largest organizations could escape bankruptcy under certain adverse conditions. In the longest strike in the automobile industry (Chrysler Corporation, 1950) the chief issue was not wages but the pension plan—the size of the proposed cash reserves and participation in administering the plan.

The actuaries are having increasing trouble in evolving sound pension plans. When mortality statistics shift in the direction of longer life, the life-insurance companies benefit but pension plans suffer. A pension contract is a promise to pay back to an individual money saved in premiums during working years, the payments to continue from a stated age until death. To be sound, the contract must be based on the ability to predict with reasonable accuracy the life expectancy of the average individual. The mortality statistics of a country are the basis for such predictions. The difficulties that unforeseen and marked changes in mortality data place in the way of the predictors are obvious.

There is another ghost at every pension feast. Pensions are essentially savings. What will the dollars saved today buy some decades hence? To say that every worker by the year 2000 will have an annual income

better prevention and treatment of infections at all ages Other medical triumphs could also be cited In the United States, a lowered birth rate and diminished immigration have served to increase the percentage of aged in the population

## ECONOMIC PROBLEMS

Of major and rapidly increasing concern are the economic problems which an aging population is creating in this country

Thrift is not a common virtue Of those over 65 only 5 per cent have saved a sufficient competency to be self supporting The rest must work or depend upon others for their maintenance But only 25 per cent of these oldsters are gainfully employed Therefore, 7 out of every 10 of those over 65 are now being supported by others Those over 65 today constitute 11 per cent of those over 18 that is 1 oldster for every 8 younger workers In 1980 they will constitute 20 per cent of those over 18 or 1 oldster for every 4 younger workers The speed with which this trend toward more aged in the population is moving can be judged from these figures between 1930 and 1940 our total population increased 7 per cent but the number of those over 65 increased 35 per cent It is clear that more and more old people must be kept by relatively fewer and fewer young people

*The basic economic needs* of all persons can be grouped under 3 headings *Subsistence* (food shelter clothing and the like) *care* (simple help from others for those unable to help themselves children the injured crippled and infirm) and *treatment* (the costs incident to illness) The aged differ from the rest of the population chiefly in their proportionately greater need for *care* and *treatment*

It is instructive to examine the ways in which these basic economic needs of the aged have been met in the past and are being met today

SUBSISTENCE —1 *By Working or Through Their Own Savings* —This is the ideal solution The sweetest bread is that which we earn by our own efforts, the bitterest, the bread of charity It is the happiest solution because it assures the oldsters of the independence of living in their own quarters No house is big enough to hold two families

2 *By the Help of Children* —The Fourth Commandment has solved the problems of the great majority of our aged in the past Let it be said that the help of children is best applied by maintaining the parents in their own homes The homes of the children are a second best choice the parents are at least not among strangers, even though they are less independent

But this solution is less available than formerly, when there were large families and big homes Today there are fewer children, and there is no room for a parent in the modern small house or apartment During 8 recent years the writer helped process about 2000 applications for admission to a large home for the aged No less than 95 per cent of the applicants had no living children As for the rest their children were either too old themselves or for various reasons unable rarely unwilling to help their parents

3 *By State Aid* —More and more government has had to step in with financial help when other sources were not available Funds have been provided by means of enforced savings and through taxation notably in the form of *social security benefits* and *old age pensions*

(Again such funds are best applied to maintain the aged in their own homes Second best are living quarters with children or friends Another type of home establishment that is increasing in numbers is the *pseudo-family* when two or more unrelated oldsters pool their resources to provide themselves with a house or apartment The problem of housing is further complicated by the widowed state of the old person it is more economical to shelter two than one in a room Yet in 1940 of men over 60 20 per cent were widowers and 10 per cent were single or 30 per cent alone Women over 60 were 44 7 per cent widows and 9 3 per cent single or 54 per cent alone )

*Social security benefits* are being increased in amounts and in groups covered Commendable though this method of support for the aged is it has a weakness to be mentioned later

of the patients now in general hospitals in Philadelphia could be cared for in their own homes if certain services were there provided by the hospitals and professional groups housekeeping help, nursing medical attention such gadgets as wheel-chairs and hospital beds laboratory service, and physiotherapy The efforts along these lines being made by certain hospitals (the Montefiore Hospital in New York the Germantown-Chestnut Hill Hospitals and Children s Heart Hospital in Philadelphia) are being watched with interest In Philadelphia the Purple Cross is an organization of registered nurses who pledge themselves each to give one day a year of free nursing service to patients at home

*The cost of treatment* can be listed under 3 headings (1) *the cost of hospitals*, (2) *the cost of hospitalization* and (3) *the cost of physicians services* The first is borne by the public the last two by the patient

The *cost of hospitals* is a complex responsibility in our economy The earlier hospitals were privately built by charitable citizens Then communities at the local level provided additional hospitals Increasing costs and unequal resources in different parts of the country brought State and Federal aid into the picture There is still a major local responsibility for the cost of hospital construction The chief governmental source of funds for this purpose is through the provision of the Hill Burton Act

An important factor in the wise expenditure of money for building new or enlarging old hospitals is the establishment of *voluntary local planning agencies* to assess local needs for and efficient use of hospital beds Such planning is as yet only in its beginnings

The *cost of hospitalization* and the *cost of physicians services* are seldom considered separately in current discussions of how the individual is to be protected against the financial stress of catastrophic illness Yet they should be for most laymen are under the impression that physicians services are largely responsible for the high cost of major illnesses and so are easily swayed to align themselves against the medical profession in considering solutions for meeting the high cost of medical care Actually the cost of physicians services are only a small fraction of the total cost of the major illness that puts a patient into a hospital

It is clear that protection of the individual against the cost of catastrophic illness can be achieved just as against any other major loss only by insurance The chief question at issue in this field today is whether this may best be accomplished by voluntary plans or by compulsion through government This in turn, raises far reaching questions not only in economics, but in the political structure and philosophy of our nation Shall we sacrifice our democratic government by shifting to state socialism? That would be the probable result of a program that begins with compulsory health insurance The events in Great Britain point that way

This all seems far from the subject of the Care of the Aged yet their increasing numbers more than any other cause have been responsible for the raising of these serious and vexing economic and social questions It is clear that there is today no single panacea for the financial problems of the aged We must study and try out various plans and approaches we must figure their costs and how and by whom those costs can be met we must remember that the costs must be kept within our means to pay

Here attention is called to a basic economic principle the standard of living of a nation depends upon the total production of its people If more and more old persons must be supported by fewer and fewer workers then a lower standard of living will result We can avoid a lower standard of living in only 2 ways increased productivity of the workers or keeping more old people at work

A major medical as well as economic problem today is how to keep more old people gainfully employed Enforced retirement is certainly not a generally desirable principle in industry There should be elastic rules to keep those in good health and physical condition at work beyond a stated age

Here industry must rise to the occasion with new programs The oldster should keep on working but not necessarily at the same job There is need for new employee groups to which only older workers are

of $5000 is meaningless if the purchasing power of that dollar is not defined Every adult today has had enough experience to know that the net result of changes in money value in the long run is inflation, not deflation

It should be clear that pensions alone can not be expected to solve all the financial problems of the aged

CARE —When an individual needs personal help in addition to basic subsistence, his economic situation becomes much more difficult *Care* costs about two and a half *times as much as does bare subsistence* when that care has to be furnished by a stranger to a single person The prolonged cost of a practical nurse for example, is beyond the means of many individuals or families and beyond all or most pensions *Care* is low in cost only (*a*) when given free by the members of the family or (*b*) when administered to large groups of needy in an institution

1 *Homes Government supported* —Government, usually at the local level (city or county), has therefore had to provide through taxation such institutions for the indigent who need care in addition to subsistence However the standard of living which obtains in such "homes" is at the lowest possible level of existence the tax payers see to that Moreover those who enter can not pick their company The *chief objection to these institutions is that* there is only one criterion for admission indigence These facts all too often combine to justify *the name that such places have* carried through the years "Poor House"

2 *Homes Privately Supported* —There will always be a need and a *place* for the "Home for the Aged" as provided by particular groups in the community a religious body a racial group, a lodge a trades union a profession, and for obvious reasons There is a personal interest on the part of the benefactors who take pride and satisfaction in their undertaking The beneficiaries find themselves in congenial surroundings among people some of whom they knew before and all of whom share common interests and a common background As a result of these facts and in spite of rising social benefits at the hands of government, there has been no reduction but a steady increase of petitions for entry into such homes of the aged in sharp contrast to the decreasing numbers of children in orphanages

TREATMENT —When illness enters the picture there is the sharpest upswing in the cost of an individual s needs The aged are victims *far out of proportion to the rest of the population In 1940 among* policy holders of the Metropolitan Life *Insurance Company the average number of* days of incapacitating illness was 6 9 a year but those over 65 were ill 35 days a year *In* a large home for the aged known to the writer, a home whose inmates have an average age of 79, the average number of days in hospital for each inmate is 91 a year

1 *Hospitals* —Little wonder then, that elderly patients today fill a majority of the beds in all our general hospitals But general hospitals are intended primarily for the acutely ill and are provided with every diagnostic and therapeutic facility this makes for the highest cost of daily maintenance It is therefore financially unsound to use such beds for those with chronic illness requiring little beyond nursing care

There is consequently a growing and pressing need for special hospitals for certain types of cases hospitals for the mentally ill, *for paralytics* for arthritics for cardiac patients and for the blind

There is particular need for a new type of *hospital facility for the aged* a glorified infirmary that would meet the nursing and simpler medical needs of its inmates but *would be close enough to a general* hospital to be served by the latter s special facilities and staff In a small community this might *be a floor or a wing of a general hospital in larger communities* a separate building in the immediate vicinity of a general hospi*tal would be better*

But it will take time and money to provide such new buildings for the care of our aged *patients The financial problems* of our general hospitals are so urgent today that earlier and cheaper solutions are being sought by *hospital administrators* Of particular promise is *the possibility of projecting hospital care into patients homes In a recent survey* the Philadelphia Health and Welfare Council found that 50 per cent

changes Bone loses some of its mineral content and appears less dense in roentgenograms Cartilage, especially over joint surfaces and in the intervertebral discs, becomes thinner so that loss in stature to as much as a couple of inches results Bad posture with increased stoop will exaggerate this loss in height

Atrophy of alveolar septa and stretching of inelastic alveolar walls are characteristic of the lungs of the aged

Liver spleen kidneys, and pancreas show increase in fibrous septa and varying degrees of atrophy of parenchymal tissues

The endocrine glands share in these changes and probably play an important role in the process of aging

The brain is longer spared than most tissues but later shows both atrophy and fibrosis Its sensory receptors however show constantly some characteristic changes and deterioration sclerosis in the inner and middle ear atrophic changes in sensory nerves Here can also be mentioned the diminishing elasticity of the crystalline lens

*Changes in Function* —There are alterations in function many of which are related to the structural changes above noted The diminished capillary bed of the skin is largely responsible for the lessened ability of the aged to stand the cold What is less generally appreciated but more important is that the same reason makes it hard for the aged to dissipate heat through the skin and so to stand hot weather It is the aged who are the first and most numerous victims of a heat wave The dryness of the skin makes it more vulnerable to the effects of soap and detergents

The blood pressure tends to rise in the less elastic arteries Diminished blood supply results in lessened function generally

In the lungs the lessened capillary alveolar area progressively limits gas interchange between blood and air and consequently limits the activity of the individual

Lack of teeth may impair nutrition both by altering the kind of food eaten and by making it less easily digestible Gastric achylia and therefore impaired digestion are common yet so frequently symptomless or so vaguely suggested as to be overlooked Constipation is common due in part to the atrophy of the smooth muscle of the intestines

Of great importance but as yet not well understood are functional changes in the endocrine glands Sexual function wanes and ceases the basal metabolic rate declines Many subtle chemical changes in all portions of the body develop in the wake of flagging pituitary function The changes in structure and function that take place gradually during aging may occur with dramatic speed in diseases in which pituitary failure plays a major role such as Simmonds disease seen oftenest in women at the menopause and progeria that disease in which the picture of advanced senility is seen in adolescents A fuller understanding of the role of the endocrines in nutrition and aging may furnish the means for influencing these processes and delaying senescence

Last to deteriorate is the mind Long after evidences of decadence are present in other bodily functions the mental activity continues if not unimpaired certainly at a high level of efficiency (Perhaps this is at least one reason why mentally no one believes himself to be old even though he is conscious of the physical limitations which aging has imposed upon him) Certain faculties wane sooner than others The ability to memorize is the first aspect of memory to lessen There is prolongation of reaction time before skills themselves are lost Impairment of vision is usual but hearing may be long preserved There is diminution of acuity and intensity of touch pain and temperature perception Tendon reflexes tend to diminish and may even disappear The pupillary reflex to light may show similar changes

There are *psychological changes* that are part of the picture of aging Here it is not easy to separate that which is normally to be expected from that which is produced by severe stresses be these incident to intercurrent diseases or to social or economic misfortunes The psychologic changes are also conditioned by the personality of the individual and his consequent ability to adjust himself to life situations Impatience and irritability are often born of the lack of understanding by others as well as the old-

eligible Jobs must be found in which these can work at a slower pace, for shorter hours, perhaps for less pay but needing less or no pension, above all being happier the while

Industry is becoming increasingly aware of the fact that the old worker has advantages that offset in variable measure his handicaps of less speed strength and endurance In his favor are experience judgment and stability Absenteeism for any reason save illness is far less in the older age groups

POLITICAL PROBLEMS — Those over 65 comprise 12 5 per cent of those over 21 the voters and in 1980 they will be 25 per cent So large a minority can decide elections

Therefore politicians are appealing to the aging voters to gain their own ends Promises are made some in good faith others evidently with no possible thought of fulfillment California found a 75 dollar pension at age 63 too expensive in 1949 yet in 1950 a gubernatorial candidate promised a 100 dollar pension Political economy is a well-known discipline, but there is no such thing as economical politics

A more sinister angle of the political problems is this the idea of the welfare state is easy to sell to the impecunious old and near old Politicians find here a means to power at the expense of democratic principles Bread and Circuses was the slogan of the Roman politicians 2000 years ago today it has been condensed to one word Security Let it be remembered that Hitler did not seize power but on the basis of promises of a better lot was voted into office in an honest election One by-product of the hand out state is reduced initiative in its citizens and a consequent lowered production that lowers the standard of living But the greatest tragedy of the welfare state is the piece meal destruction of personal freedom

PHILOSOPHICAL PROBLEMS — Some believe that the increasing proportion of aged in the population will lead to greater conservatism in outlook and action with less chance for error but also less advance This is open to question, since the aged are inclined to take chances and because they can consider impartially the long range plans beyond their own life span Perhaps the benign influence of the women will play an increasing role since they are living longer than the men their life expectancy at birth today is 69, as compared with 66½ for the male Thus in 1930 among those over 65 there were 118 women for every 100 men In 1940 this ratio had increased to 124 100

## MEDICAL PROBLEMS

What has thus far been said in this chapter has the purpose of bringing into proper focus and perspective the problems that face the physician in his care of the aged It is not just a matter of the prevention diagnosis and treatment of disease in an old person, nor the attempt merely to prolong life Much more is it the preservation of health and efficiency as long as possible The goal in the words of Stieglitz is to put more life into years not just more years into life

*What is Old Age?*—It may be adumbrated rather than defined as the inexorably accumulating sum of a series of deteriorative changes in structure and function subtle and minimal in their beginnings yet eventually so marked and obvious as to be universally known and recognizable

*Changes in Structure* —The commonest structural change that characterizes the process of aging is atrophy It occurs in practically every organ and tissue save only the heart which is usually late and last to show it With it frequently goes a replacement of more vital cells by fibrous tissue The more important anatomic changes are the following

The skin loses much of its capillary bed its fatty panniculus diminishes its hair loses pigment whitens falls out and its specially functioning structures (sweat and sebaceous glands hair follicles) are undernourished atrophy and may in part disappear At the last the skin is thin wrinkled dry pale and cool Mucous membranes have comparable changes with loss of teeth and with diminution in numbers of secretory glands

Blood vessels more especially the arteries become less elastic somewhat lengthened and even tortuous

Muscles atrophy generally not only skeletal muscle but also the smooth muscle of the digestive tract

Bone and cartilage show characteristic

as exemplified by racial or local groups with divergent records for longevity Deficiencies of vitamins or minerals may be as important in speeding senescence as in delaying growth There is accumulating evidence that atherosclerosis may be related to the ratio between cholesterol and lipids in the diet The availability of fluorine in childhood determines the durability of the teeth The possibilities for investigation experimental statistical and clinical of the relation of nutrition to aging are among the greatest in all contemporary medicine

Closely allied to and frequently inseparable from nutrition is the role of endocrine function in the processes of senescence Here too our knowledge is fragmentary and theoretical But chemistry is opening avenues that should lead to surer ground than have the cruder methods of the past

In the realm of the psyche, early influences have an important bearing on mental problems in the aged Personality is the combined product of heredity and of conditioning experiences in early life Therefore attention to mental hygiene in youth will pay dividends in better adjustment and greater happiness in old age

All through life there are stresses whose effects on tissue and function must be far-reaching Infection is at times the obvious cause of a dramatically premature aging in an organ or organs Less obvious but cumulative may be the effects of minor but repeated infectious insults Or conceivably there may be favorable effects from symbiotic organisms It is not too far a cry from Metchnikoff s theory of longevity as related to the intestinal flora to the role of fungi (*e g* penicillin) in the control of infectious diseases today

Heredity is the chief factor in determining the anticipated life span of an individual Thus far little is known of its mode of operation yet one may well hope that it too may be influenced more directly and immediately by chemical means (*e g* nutrition) Valuable as have proved the methods of breeding in modifying heredity in plants and animals their application in man eugenics has been minimal and the results negligible

## WHAT CAN BE DONE TO PROLONG LIFE?

One evening the writer sat next to a prominent surgeon, past 70 in years but so much younger in mind and body that he could have claimed the late fifties When asked his secret of perpetual youth, he answered 'That s easy Meet this gentleman my father he s 93 The importance of heredity in aging as well as in life expectancy is well shown by the observations of Kallmann and Sanders in 1 602 twins In the monozygotic (uniovular) twins there was a striking parallelism not only in the length of life of each of the pair but in the time and manner of aging in various organs and tissues, and in the cause of death Dizygotic twins varied as widely in all these points as did any non twin siblings Unfortunately we can do nothing as yet about heredity

Yet there is promise that someday something may be done to influence heredity If any one of a hundred bee larvæ is fed for only a few days in its early existence some 'royal jelly a substance produced in the throats of worker bees and extremely rich in pantothenic acid, the larva so fed will grow up to be a queen the rest will become workers A worker bee lives one year a queen bee five years Rats fed an omnivorous diet live longer than litter mates raised on a vegetarian regimen Rats also live longer if semistarved than if overfed Evidence is accruing that fat in the diet and hereditary weaknesses in metabolizing fats are related to atherosclerosis Therefore predictions are reasonable in promising a delay in vascular aging and a longer life span by controlling the cholesterol lipid ratio in the diet

Today the physician s efforts are primarily to be directed to help an individual to live out his expected life span efficiently and happily This involves not only the prevention and treatment of disease but instruction and guidance in a proper mode of life Naturally this mode of life must be cultivated in earlier years to achieve its results For descriptive purposes however it will here be called

*Hygiene for the Aging and the Aged* —The program of living best calculated to insure

ster s own physical limitations In any event old age brings with it a sobering influence on the psyche that may variously find expression as conservatism fatalism lessened enthusiasms and heightened pessimism

To practice medicine intelligently among the aging and aged, the physician must have a knowledge not only of the nature of the changes in structure, function and psyche that are incidental to aging but also of the order in which, and the time of life when those changes may be expected to appear His problem is comparable to that of the pediatrician who has had to work out a timetable of height weight structure-function intelligence factors in relation to age from birth to puberty

But the problem in geriatrics is much more complicated than that in pediatrics A major difficulty is to distinguish between that which is normal aging and that which is exaggerated and pathological change For example when is vascular change the disease arteriosclerosis rather than fibrosis in keeping with the individual s age? In general a helpful guide is to consider structural changes normal so long as they do not interfere with function for that age Then too, one must consider the hereditary background of the individual in deciding whether a given change in structure or function is timely or premature for that person

Especially in the realm of mind and psyche is it hard at times to distinguish between the normal and the abnormal Forgetfulness in little and recent things is an early and constant finding in senescence But it merges imperceptibly into pathological loss of memory An old patient of the writer s knowing that she might fail to tell or ask him about something at the time of his visit used to keep notes to compensate for the forgetfulness that her 80 years justified But eventually she could no longer remember what she had written on one side of the paper and so repeated her questions *on the other* side Pessimism and worry may be fully justified in the light of impending poverty loss of employment or illness But such emotions may be magnified out of all proportion into miserliness that causes an individual to starve when he has many thousands of dollars in the bank, or into a depression that leads even to suicide

Nor can one decide whether a given emotional reaction is normal or excessive without full knowledge of attendant circumstances It is easy to overlook *loneliness* as a justifiable cause of a psychological pattern A major trial in old age is the loss of one s spouse and contemporaries and therefore of one's confidants, companions and friends This is as true of the rich as of the poor and they can be more lonely and uncared for spiritually in the homes of their own children, with whom they live but whose lives they do not share than if they lived alone in a hall bedroom

The elderly all too often make matters worse in their environment by their own intransigeance Not realizing that they may be more of a liability than an asset in the household they fail to make any effort to offset this by being pleasant in manner or thoughtful in action As Thewlis has put it with brutal frankness the aged are often economically useless esthetically repulsive and temperamentally difficult In consequence there may be a hostility hidden or overt on the part of one or more members of the household against the oldster To loneliness is added discontent Suppressed emotions find expression in symptoms and complaints All this must be considered by the physician in assessing the psychological status of his patient

## THE MECHANISMS OF AGING

Although it would be naive to put the question What are the causes of old age? it is highly proper to inquire into *the mechanisms of aging* Just as there are many factors which are known to retard, alter or speed up the processes of growth and maturation so there must be many factors that similarly influence the processes of decadence at the other end of life Our *knowledge of them is as yet in its beginnings* and herein lies a fruitful field for research

Some leads are now apparent Nutrition covers a most important group of clues These include deficiency factors and diet composition not only over the years but especially at critical period in early life or

should they be multiple rather than a single vacation annually Except for the hottest part of the year it matters little in which season the holiday is taken

*Diversion* —An indispensable ingredient in the formula of growing old happily is the possession of a wealth of inner and spiritual resources with which to occupy the increasing hours of leisure Diversion unfortunately is today too often considered synonymous with amusement and amusement is becoming increasingly of the passive variety Radio television and reading of the newspaper — of the comic strip variety — are robbing us of our capacity for active diversions Yet it is far more soul satisfying to make music than to listen to it to draw a picture or model a figure, or even to whittle on a stick to study some new subject or read a thought provoking book article or editorial or to argue a timely topic with a friend all this for at least a part of the time rather than to sit idly while others act feel and even think for us

But to do such things in our old age and especially to do them well we must learn how to do them when we are young Old age is something that everyone expects to attain Moreover most persons now being born will do so Therefore education and training in youth certainly as early as the high school level should include this aspect of preparation for life

The most valuable education is one which not only teaches an individual how to think and study but how to continue self-education by self imposed disciplines after formal education ends That goal is rarely achieved even at collegiate educational levels today Yet in such self instruction lies a great source of happiness and satisfaction in the ever broadening mental horizon which it can bring throughout life, even when physical infirmity builds its increasing limitations

Therefore it is significant that public school systems are beginning to experiment in adult education by evening classes in the school buildings They are offering a wide range of subjects but with emphasis on cultural topics and the art of living Herein lies real promise for education is a never-ending process not something that like growth must stop with most people in their teens In fact there should be better results with adult students than are achieved in our schools and colleges with teen-agers We have proof of this in the records of G I students as compared with those of their less mature classmates

A major tragedy in old age is the progressive loss of one s contemporaries This must be compensated for as well as may be by regularly making new and younger friends, lest loneliness become overwhelming The youngest old people are those who preserve a fresh outlook on life by cultivating contacts with the young

Diversion then in old age depends in large measure on the inner resources that have been accumulated by the individual in his earlier years The greater those resources, the less is he dependent on others for diversion But much can be done to plan group activities for the aged Such programs are now being tried at community levels as a welfare activity with a full time staff to organize groups under volunteer leaders in clubs churches neighborhood centers to participate in entertainment social gatherings lectures musicales games and handicraft An important benefit is the opportunity to make new friends A fertile field for trying out such group activities is furnished by the homes for the aged that now shelter over half a million persons The chief lack here as the writer has found is of trained social workers who have had experience in working with groups of the aged

It must be emphasized that to work to best advantage and to enjoy diversion to the fullest the aged must be provided with proper glasses hearing aids and dentures This seems obvious but the aged are all too often unable to provide these for themselves and hesitate to ask others to do so It is the responsibility of children and other relatives to make such provision and it is up to the physician to remind them of this responsibility

*Moderation* must constantly be stressed in advising both the aged and those who look after them Moderation applies not only to work rest and diversion but also to diet habits and personal hygiene

evenness as well as slowness in the progression of aging consists of work, rest and diversion, in proper balance and governed by the watchword of moderation in all things

*Work* is a prime means to preserve vigor The wheel which doesn't turn, rusts An old Navy regulation in the case of ships out of commission called for jacking over the main engines one and a quarter turns every 24 hours Faculties and skills as well as muscles that are not used weaken and atrophy Therefore work calls for some physical and mental exercise, as well as exertion in as many activities as the individual can reasonably engage in as often as feasible

But work is more than a means of keeping body and mind vigorous It is the most important key to happiness A major step in the transition from immaturity to maturity is the realization that work in itself is enjoyment By the same token, continued happiness in old age is assured as long as there is work to do and enjoy Work is the best thing to give life an enduring purpose Without purpose life is not only futile, but becomes a burden Therefore work must be a part of daily life as close to its end as may be

The problem of finding work of a type that the oldster can perform has medical as well as economic aspects In our hospitals we see all too often the wrecks that result when a person persists in an occupation that is beyond his waning capabilities Necessity may have been the driving motive, but proper advice by a family physician might have convinced him of the value of half a loaf We learned in war time that even old automobiles lasted many years as long as they were driven at moderate speeds but broke down promptly after the war when speed restrictions were removed For the same reason any exercise in which the individual engages must be suitable in type and degree to his ability to perform

The work done must itself have a purpose be that purpose ever so humble or simple It should be remunerative if the worker is not financially independent It is not so much a matter of the amount of the pay its value to the morale of the oldster is far beyond the dollars and cents involved Even in homes for the aged it has proved worth while to reward the guest for small chores performed to be able to jingle in his pocket a few coins he has earned is a great boost to his self respect

Retirement may be at the individual's choice In that case he may ask his physician "When shall I retire?" The important question however is not when to retire but what to do in retirement That question is easily answered by the man with many interests He can substitute his avocations and hobbies for his former job He can look forward to retirement as a welcome relief from less interesting work drudgery by comparison with doing the things for which up to now there has been little time But the question of what to do in retirement is a tragic one for him who has known only his job Riches alone are no solution In fact all too often the rich man has devoted himself so entirely to the making of money that he knows nothing else He thinks he will now turn to a hobby But hobbies should be started in youth and constantly cultivated through the years if they are to serve well later on (Let physicians themselves take note)

*Rest* in the proper doses is an increasingly needed restorer in later years The old need in the aggregate more sleep than in middle life But that does not mean that they need it all in one piece Since they tire easily, they are prone to indulge in several naps during the day This more than accounts for shorter sleep at night as a rule Yet this has given rise to erroneous claims by many old people that they sleep less than they did formerly The myth of Edison's 4 to 6 hours of sleep a day was dispelled after his death by the report of his laboratory staff who clocked his naps and found that he slept at least 8 hours in the twenty four

It is sound practice for the elderly to observe an early afternoon siesta This should be made a part of the routine of the working day Horizontal rest with or without sleep will improve efficiency in the latter part of the day and will avert the excessive fatigue that follows a day of unbroken activity

Vacations should be observed in longer periods with advancing years Even more

should they be multiple, rather than a single vacation annually. Except for the hottest part of the year, it matters little in which season the holiday is taken.

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But to do such things in our old age and especially to do them well, we must learn how to do them when we are young. Old age is something that everyone expects to attain. Moreover, most persons now being born will do so. Therefore education and training in youth, certainly as early as the high school level, should include this aspect of preparation for life.

The most valuable education is one which not only teaches an individual how to think and study, but how to continue self-education by self imposed disciplines after formal education ends. That goal is rarely achieved even at collegiate educational levels today. Yet in such self instruction lies a great source of happiness and satisfaction in the ever broadening mental horizon which it can bring throughout life, even when physical infirmity builds its increasing limitations.

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Diversion then in old age depends in large measure on the inner resources that have been accumulated by the individual in his earlier years. The greater those resources the less is he dependent on others for diversion. But much can be done to plan group activities for the aged. Such programs are now being tried at community levels as a welfare activity, with a full time staff to organize groups under volunteer leaders in clubs, churches, neighborhood centers, to participate in entertainment, social gatherings, lectures, musicales, games and handicraft. An important benefit is the opportunity to make new friends. A fertile field for trying out such group activities is furnished by the homes for the aged that now shelter over half a million persons. The chief lack here, as the writer has found, is of trained social workers who have had experience in working with groups of the aged.

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*Moderation* must constantly be stressed in advising both the aged and those who look after them. Moderation applies not only to work, rest, and diversion, but also to diet, habits, and personal hygiene.

*Diet* —The two most important dietary rules (and the two most commonly broken) are (1) that the caloric intake not be excessive and (2) that the diet be properly balanced

Obesity is the commonest disease in the United States The aged are particularly prone to it when one by one other physical pleasures have been outlived or denied and there remain only the joys of the table Yet obesity itself is the greatest single threat to longevity, as all mortality statistics show

Unbalanced diets are extremely common among the aged if the choice of food is left wholly to them This may be because poverty makes proper selection difficult or because poor dentition limits the range of acceptable foods or because the oldster yields to likes and caprice even more than do children and without the control that safeguards the latter, or because it is just too much trouble to cook a proper meal or to go out to eat Tea and toast diets are all too frequent Proteins and vitamins are commonly in inadequate supply Every form of dietary deficiency and in every degree is therefore encountered in the aged and represents another serious threat both to health and longevity Neither intelligence nor knowledge will always protect an oldster from falling into such foolish error This and the fact that such deficiency diseases in the elderly are easily mistaken for organic disease of other origins is shown in this example

A retired professor of a school of medicine wealthy, keen mentally robust in body, and well adjusted mentally (except perhaps that he was a bachelor and lived alone in a large house), began in his seventies to fail in health and strength, and *finally was admitted to a* hospital apparently in the last stages of some organic, probably malignant disease He was profoundly anemic edematous and lethargic *Yet after* transfusions symptomatic medication and proper feeding he rapidly returned to good condition and no organic disease could be found It then developed that for many months he had eaten nothing but tea and toast

The elderly, therefore need help and supervision in the selection of their diet Dental deficiencies must be *remedied* *Solid* foods that defy their dentures should be properly comminuted before being served Failure to do this is the commonest and most costly mistake made in *food service in* hospitals if any one doubts this statement, let him note the untouched meat on the outgoing tray in any hospital ward The trouble is that internes *residents and* nurses the people who order or serve the diets still have their teeth and so do not appreciate this handicap of the aged Moreover hamburg steak is much cheaper than tenderloin and just as nutritious

*Alcohol* is allowable in moderation It may stimulate gastric secretion and a flagging appetite If there be a threat of overeating, then an after-dinner highball can replace the pre dinner cocktail The vaso dilating and sedative effects of alcohol have actual and pleasant therapeutic value, as for example in mild angina But it is not well to prescribe alcohol for one who is opposed to it other and cheaper medicaments are available Excesses are not to be condoned, but one is reminded of Pepper s story about Benjamin Franklin then in his eighties who in remonstrating against his physician s order to give up alcohol pointed out that one sees more old drunkards than old doctors

*Tobacco* in the presence of heart disease especially coronary involvement and in case of peripheral arterial inadequacy should be prohibited Otherwise smoking should be allowed in moderation Here, too it is wise to ration the daily allowance *of the very old for they easily become chain* smokers Never should they be allowed to smoke in bed unless under supervision

*Sexual Intercourse* —Nature sets its limitations *in most instances* Here too moderation is the watchword But there comes to mind the old saying that an old man s three worst enemies are a well stocked wine cellar a good cook and a young wife

*Bathing* —The old should not be required to bathe oftener than once or twice a week The de fatting effect of soap on their dry and atrophic skin leads easily to eczema

*Care of the Bowels* —Constipation *is* common among the elderly So too is forgetfulness and this may give rise to an errone

ously high estimate of its severity. There fore some simple way of recording a bowel *movement* should be used. To relieve constipation, a mild laxative is far preferable to the indignity of an enema.

*Urination*.—Tycho Brahe, the great astronomer, lost his life because he feared to excuse himself in the presence of the Emperor of Austria and so developed acute retention. All old men and especially those with beginning symptoms of prostatism should void frequently. The writer remembers the advice received as a youngster from his family doctor, then in his eighties (B. I. Hinkle, Class of 1846, University of Pennsylvania): "My boy, void whenever you get the chance, whether you feel like it or not—you never know when the next chance is coming."

## SOME ADVICE TO LAYMEN WHO ARE RESPONSIBLE FOR THE AGED

This applies especially to children and other relatives of the aged.

The aged are best cared for and happiest in their own home. But if because of infirmity they must be moved into the home of a relative, or if the lone survivor of a couple must be so moved, then the room to receive them should be furnished as far as possible with things from the old home—pictures, trinkets, favorite chairs and table or desk—they are ties with the past. That room should be their palace, never to be entered without their permission, and to be treated as the symbol of the privacy that should be theirs.

Under no circumstances should a couple be separated. It is sheer cruelty even to send one parent to one child and the other to another.

The aged should be encouraged to continue and foster old friendships and old interest in their new surroundings. They and their friends should also be invited to some of the parties and functions of the household. They should be stimulated to do things and go places—to church, to club or lodge, to meetings, and to observe anniversaries and significant occasions.

They should be provided with some spending money, and preferably under some arrangement, even subterfuge, that it is something due them, in order to uphold their self respect. For the same reason they should be encouraged to observe neatness in dress and personal appearance. Nothing is so flattering as to seek their opinion and advice.

They should be given the chance to be useful by doing things in the household. Yet the bitter feeling of utter uselessness that plagues the aged is so often made worse by the young who find it easier to do something themselves rather than wait for it to be done by the aged. Even trifles mean much to them: for a decade an old man was happy in winding and regulating the clocks in the home, and he beamed each time they struck in unison.

Above all, they should be shown signs of affection. They are happiest in the knowledge that they are loved and welcome.

*Care During Illness*.—The aged person when ill should not be hospitalized unless circumstances demand it. His morale is best at home. The mention of hospital all too often strikes terror to his heart. Of course, if because of previous favorable experience he asks to go to a hospital, that objection is removed.

Whether at home or in hospital, the aged patient requires nursing care at night. Delirium, particularly during acute infections, tends to come on at night, although the patient be quite lucid throughout the day. Mental confusion, even in the absence of severe illness, is common at night, especially when an individual who has recently been moved to new quarters awakens and imagines himself elsewhere. Whether delirious or confused in the night, the oldster may get out of bed and do foolish or dangerous things. *In his attempt to go to the* bathroom as remembered in a former home or in an act of delirium, he may fall with serious or fatal result. Therefore, during severe illness a night nurse is more important than one by day. Always, whether well or ill, the oldster should have a *night light* burning, so that he can promptly orient himself.

Whenever possible, old patients should be

given bathroom privileges If that be not feasible, then the use of a commode at the bedside is still much less exhausting and much to be preferred to a bed pan

## SOME EFFECTS OF AN AGING POPULATION ON MEDICAL PRACTICE

The increasing percentage of the aged in the population is making changes in the complexion of the medical practice of today as compared with that of a generation ago Two noteworthy aspects of such changes are seen (1) in the greatly altered incidence of the kinds of diseases and (2) in the more subtle shift in the clinical picture of individual diseases

*Changing Incidence of Diseases* —In 1900 the nine leading causes of death were in this order (1) pneumonia and influenza (2) tuberculosis, (3) diarrhea (4) heart disease (5) kidney disease, (6) apoplexy, (7) cancer (8) bronchitis, (9) diphtheria In 1940, the list read as follows (1) heart disease (2) cancer, (3) deaths by violence (until 1948 the chief manner of violent death was by automobile but in 1949 this was the second cause of violent deaths the first being accidents in the home the elderly were responsible for this shift—in 1949 theirs constituted 40 per cent of the accidental deaths, of these 60 per cent were due to falls, and 86 per cent of the falls occurred in homes) (4) apoplexy (5) kidney disease (6) pneumonia (this will be much lower in 1950 statistics) (7) tuberculosis (8) prematurity (9) diabetes (in 1900 this cause was 27th on the list)

*Different aspects in the clinical picture of the same disease* are at times presented by the aged as compared with younger patients Diminished sensation modifies symptoms Fractures, lacerations and operative wounds are less painful and therefore early ambulation is easier with old patients Biliary colic is decidedly less common in the aged Gall stones may cause no pain even when they ulcerate through the gall bladder wall into the small intestine, which they may obstruct in the last foot of the ileum Turner has reported a case in which the ulceration occurred into the colon which was then obstructed by the stone measuring 2½ by 3 inches and weighing 5 ounces Peptic ulcers may be painless and unrecognized until they perforate or bleed Renal colic is often less severe As Rolleston has said, The organs in the aged suffer in silence

## SIGNIFICANT FACTS ON CERTAIN DISEASES AS SEEN IN THE AGED

Attention will now be called to some useful clinical facts about various diseases as they occur in the aged They will be taken up in some order by systems and groups There will be no complete descriptions of any disease that would be duplication of material in other sections of this textbook The purpose here is rather to give emphasis and perspective

*Old Age Itself* —Is old age a disease? No Ideally it is the natural cause of death a wearing out equally in all parts, like the one horse shay, an end without suffering, a falling asleep the old man, dozing in the sun sleeps more and longer and finally fails to reawaken Shelley has beautifully expressed it in Queen Mab '

Mild was the slow necessity of death
The tranquil spirit failed beneath its grasp
Without a groan without a fear
Calm as a voyager to some distant land
And full of wonder, full of hope as he

Like so many ideals this one too is rarely achieved Karsner made the comment that in 19 000 autopsies performed he had never seen a case of such natural death

*Cardiovascular System* —The cardiovascular diseases far outweigh in numbers and severity all others among the aged The chief ones are arteriosclerosis generalized and in local areas notably the cerebral apoplexy and myocardial sclerosis the arrhythmias coronary artery disease hypertension Since they are commoner in the aging than in those in earlier life their descriptions as found elsewhere in this work need no elaboration here

There is however an insufficient appreciation of the frequence and seriousness in the aging and the old of intravascular clotting and its consequence *thrombosis*

*and embolism* Coronary and cerebral thromboses are well enough recognized but more frequent and more often fatal are thromboses in numerous venous channels (leg veins hemorrhoidal and pelvic veins) and their secondary lesions in the lung Barnes has reported that 16 per cent of surgical deaths occurring in the Mayo Clinic are due to pulmonary embolism and infarction The routine use of preoperative anticoagulant therapy has prevented a fair proportion of such fatalities and the best results are noted in those over 60 years of age

In the arterial tree *mesenteric thrombosis* is one of the commonest of acute intra abdominal catastrophes in the aged Its greatest danger lies in delay of recognition and treatment Among the major triumphs of surgery in the aged are the patients who survive with ease the removal of large sections of intestine

*Kidneys* —Nephritis is comparatively rare in old age even though nephrosclerosis is frequent Therefore, in the presence of uremia in an old person, one should think first of an extra renal cause—some type of obstructive uropathy such as prostatism, stone benign or malignant tumor or stricture *Hematuria* is rather common In its presence, malignant disease must be ruled out, but it is frequently of benign origin—simple capillary hemorrhage such as not infrequently occurs in the skin or conjunctiva of the aged from slight trauma It is also at times associated with hypertension, much as is nose bleed Stengel used to emphasize this point in his teaching by the term *renal epistaxis*'

*Gastrointestinal Tract* —*Cancer* continues to be the most serious condition involving the digestive tract even into advanced years Its commonest sites are stomach, rectum and cecum Other parts of the colon the pancreas and the biliary tract account for many cases It should be emphasized that in the very old cancer tends to progress more slowly and is often latent Gastric cancer may become evident only through its metastases' In the cecum cancer by constant trickle bleeding brings about severe degrees of anemia that suggest blood dyscrasia especially Addisonian anemia, while the lesion is still relatively small

*Diverticulitis,* acute and chronic produces a variety of clinical pictures with elements suggesting infection, obstruction or neoplasm It is indeed a frequent precursor of cancer in the colon, where a third of such lesions surgically removed show carcinoma

*Appendicitis* in the aged tends to develop its symptoms less precipitously and so may simulate intestinal obstruction

*Gastric achylia* is the commonest abnormality in the digestive tract It is so often symptomless that its importance tends to be underestimated Yet it is essentially an evidence of atrophic gastritis It probably influences nutrition to a degree greater than is now recognized At times it gives rise to flatulent indigestion and to diarrhea It is often present in chronic gall bladder disease and may be a precursor of gastric cancer

*Acute (viral) hepatitis,* both the infectious and the homologous serum variety is not rare in the aged It tends to be more serious and protracted than in earlier life

*Respiratory Tract* —Chronic *bronchitis* is common in old age, and oftener on a less serious basis than in younger persons mild bronchiectasis poor circulation chronic infection, low-grade allergy associated paranasal sinusitis and excessive smoking are the most usual causes Nevertheless every case must be thoroughly studied to rule out more serious disease Roentgenography and bronchoscopy with aspiration of bronchial washings and examination of this material for malignant cells should early be employed to rule out tuberculosis and neoplasm

*Pulmonary tuberculosis* continues to be a serious problem in the aged not only from the individual point of view but especially from the standpoint of public health The highest mortality rate from this disease at any time of life is that of males over 65 Their fibroid phthisis moves slowly so that the true diagnosis goes unrecognized for months or years In the meantime the oldsters with their chronic bronchitis are careless in the disposal of sputum and so endanger all in the household Even when the diagnosis is made the patient often refuses to be isolated in a sanatorium

*Pneumonia*, lobular and lobar, is common among the aged though antibiotics and chemotherapy have been highly effective against it most of those who die of pneumonia are old people One reason for this is that *pneumonia may go unrecognized* longer in aged than in other patients It is an old observation that pneumonia in the aged and in the insane, may be practically afebrile The clinician who has once been embarrassed at the necropsy table by a full blown pneumonia that he had *never suspected thereafter examines more* carefully and regularly the lungs of his aged patients

*Endocrine Diseases —Diabetes* is the commonest endocrine disorder in the aged Its relative mildness and lack of symptoms are responsible for the fact that so many cases *are unrecognized their number in this* country is estimated at one million In hospitals which they enter for intercurrent disease, especially surgical conditions elderly diabetics are often unrecognized as such A urine specimen, collected in the early morning according to the usual hospital *routine is negative for sugar because of the* preceding all night fast But in the wake of the operation, the patient s sugar tolerance abruptly falls and in the obese, there may then develop an acidosis The diagnosis is established by the next examination of the urine It would be better to collect routine *urine specimens in hospitals an hour after* the main meal In the general population, there is need for yearly surveys especially among the elderly to discover the mild cases in order that proper treatment may forestall the various complications of diabetes In 1949 a radio program sponsored by the Philadelphia Diabetes Association brought several hundred new cases to hospital clinics

*Thyrotoxicosis* is not uncommon in old age It may present diagnostic problems especially if the gland is not *large* and *the eye signs* are minimal or absent In such cases the patient usually presents himself because of some secondary manifestation such as tachycardia, auricular fibrillation weight loss, or diarrhea, which may lead to an erroneous diagnosis of heart disease dysentery, or hidden neoplasm In the treatment of thyrotoxicosis in the aged, an important principle must be kept in mind it is dangerous to let the disease continue uncontrolled, lest the heart suffer irreparable damage Hence the best treatment is that which most promptly ends the thyrotoxic state Unless there are other contraindications this means surgical treatment, after the usual preparation In selected cases, it may be safe to use radio-active iodine, but it is not yet possible to assess its carcinogenic effect in the nodular goiters which occur in greater proportion among the aged

*Hypothyroidism* is also encountered in old age It may be mistaken for circulatory failure because of fluid retention bradycardia and mild breathlessness It must be remembered that pitting edema and effusion into the serous cavities including the pericardium may be due to hypothyroidism Another serious diagnostic error may arise in hypothyroid cases in which various mental symptoms chiefly depressive, are exhibited and are believed to be psychotic

Failure of sexual function is a normal accompaniment of aging But the worry which this engenders in some persons is of *pathologic importance The treatment is* by psychotherapy The attempts to restore potency and libido by measures ranging from the administration of hormones to glandular transplants are of doubtful value Even if they proved very successful one might still question the wisdom of putting *new wine into old bottles*

*Disorders of Metabolism and Nutrition — Obesity* is the chief menace to longevity, as well as the commonest disease in our population Its harmful effects on the cardiovascular system the pancreas the liver and the joints become greater with each advancing year Yet the older the patient, the harder it is to treat obesity Due almost always to eating too much obesity tends to increase as appetite continues unabated the means *to indulge it grow exercise diminishes* other pleasures become limited and (worst of all) the will to guard form and figure atrophies The treatment of obesity is important at any time but is most effective *before aging* has begun Its effectiveness depends of course upon the willingness of the patient to cooperate But the first responsibility lies with the physician who must record the

patient s weight at intervals, note early any trend to gain and then convince the patient that something must be done about it To do this, he may have to be brutal in telling the patient that he is digging his grave with his teeth

*Gout* is more frequent in the elderly than in any other group Its recognition is not difficult provided the physician is alert to the possibility The chief diagnostic stumbling blocks are (1) the simulation of rheumatic fever by early multiarticular attacks (fever leukocytosis rapid sedimentation rate) or other types of arthritis and (2) the fact that the blood s uric acid levels are usually normal except for short peaks that occur just before symptoms develop and have passed by the time the patient is first seen A therapeutic test with colchicin is most helpful

*Deficiency states* of various types and degrees are common in the aged Management of these states in the aged is the same as management of such states in younger persons

*Blood Dyscrasias* —*Anemia* is common in the aged and in its moderate forms usually has a dietary cause In the main it is anemia of the hypochromic microcytic variety Addisonian anemia may occur late in life Anemia is often secondary to neoplasm so that this differential diagnostic problem is presented by every case The anemia of neoplastic disease may be due to blood loss to depression of the bone marrow by toxic tumor products or to encroachment on the marrow by metastatic tumors, chiefly from prostate breast or thyroid or by primary tumors such as myeloma *Aplastic anemia* either primary aplastic anemia or that due to marrow exhaustion from other causes is relatively more frequent among the old than among the younger age groups *Chronic leukemias* are not uncommon In the old however they tend to progress more slowly and have longer remissions (especially is this true of chronic lymphatic leukemia) than is the case in younger patients *Acute leukemias* are rare Coagulation defects are infrequent but *purpura simplex* probably due to change in capillary walls and perhaps of dietary origin is not uncommon

*Skeletal Diseases* — *Arthritis* especially hypertrophic osteoarthritis and to a lesser degree rheumatoid arthritis, are diseases of advanced years A common bone disorder in the elderly is *osteoporosis* In part this is related to failing gonad function and suitable replacement therapy has proved helpful A major cause however, is disuse Long periods of confinement to bed are particularly likely to accentuate this trouble Ambulation and use, on the other hand are followed in a few weeks by perceptible recalcification It is futile to give calcium orally even in large doses *Paget s disease* occurs predominantly in later years there is neither a known cause nor an effective treatment Fortunately the progress of the disease is slow as a rule in those who continue to be active *Back pain* due to acute and chronic disorders of intervertebral discs is common in the old this explains many of the so-called cases of lumbago There is more virtue in preventing back pain than in curing it and this may be accomplished through regular exercises to keep the back muscles in condition and the avoidance of sudden and unusual demands on the back (the lifting of heavy weights strenuous work or exercise when not in condition and the like)

*Infectious Diseases* —Except for pneumonia and influenza infectious diseases are relatively uncommon among the aged This may be due at times or in part to acquired immunity but is usually due to infrequent exposure to infection For the aged may live long enough to lose an immunity acquired in childhood more grandmothers die of whooping cough for example, than do grandchildren In general the aged are rather poor risks when they do contract acute infections Tuberculosis in the aged has been discussed Syphilis in the aged is comparatively rare and its manifestations are less severe in them than in patients under 60

*Allergic Diseases* —Since easy sensitizability is the inborn defect that characterizes all allergic individuals the manifestations of allergy may begin as well as be present at any time of life Allergic diseases in the old however often differ in incidence,

type, and severity from such diseases in younger persons

The allergic person tends to lose some of his sensitivities as he grows older and to acquire fewer new ones There are several reasons for this It is the natural history of allergic disease that the intensity of a given sensitivity tends to wane in time and drop below the threshold level for the development of symptoms This may be through natural hyposensitization due to repeated small exposures It may be a matter of less frequent exposure because patients learn to avoid their allergens At all events, allergic diseases are generally less frequent in the aged than in the young

Certain types of allergic disease are less common than others among the old This applies especially to some of the more acute manifestations, such as hay fever urticaria, and migraine, and to food allergies Allergic digestive symptoms and headaches are also less common among the old the patient has learned to recognize and avoid the causes Contact dermatitis is less frequent too for in the old, the exposure incident to occupations is less varied and less intense

*On the other hand, some allergic disorders* occur with increasing frequency in the aged Their dry skin is likely to be subject to *allergic pruritus* and to *eczema due to various* sensitivities And though food allergies are less frequent among the old, there is greater exposure and hence *greater sensitization to drugs* among them The commonest drugs used by the aged are laxatives and phenolphthalein is an excellent sensitizer *Penicillin* sensitivity is rapidly increasing among persons of all ages, thanks to its routine use in every minor infection The serious reactions to gold in arthritics are also on an allergic basis

*Perennial nasal allergy* is frequent among the aged although not much complained of by the patient who has come to take his sneezes rhinorrhea and nasal blocking for granted It is also often overlooked by the physician who does not directly inquire about it The allergens most usually causing it are the inhalants, especially *the dust in* the patient's own home Common, too are the nasal complications of such long standing nasal allergy paranasal sinus infection and mucous polyps

Chronic respiratory infection and consequent bacterial sensitivity are *frequent in* those with perennial respiratory allergy This is responsible for the fact that *asthma* in the aged is more often continuous and chronic than it is in younger persons Infection tends to dominate the clinical picture chronic cough, purulent sputum recurrent low-grade fever exacerbations of asthma in the wake of acute colds

At this point a fact most important to the diagnosis of allergic diseases in the aged must be mentioned *the diminished reactivity of their skin to test materials* The reactivity of the skin to a given allergen decreases with the advancing years and may actually fail entirely, even though exposure of an extracutaneous shock organ to that allergen may still cause symptoms (for example goose feathers may cause asthma even though the skin reaction to them is negative)

Failure to understand this has given rise to the unfortunate and largely erroneous notion that asthma may be subdivided into *extrinsic* asthma (due to allergens outside the body) and *intrinsic* asthma (*due to a* cause within the body, notably infection) The frequent failure to get positive skin *reactions from elderly asthmatics* and the frequency of chronic respiratory infection in the aged have led to the assumption that *asthma* which begins late in life is practically always *intrinsic*—that is infectious and nonallergic in origin This is far from the truth

Sensitivity to external allergens if properly and thoroughly sought for can be established in most patients whose asthma begins in old age and such sensitivity should be suspected in the rest A frequent mistake is to assume that a patient whose asthma began in his advanced years is probably not an allergic person Yet questioning will often uncover other manifestations of allergy (excessive sneezing for example) that have troubled the patient since his early years and may even point to the probable nature of the allergens that now affect the bronchial tree in addition to the nose The frequent role of infection in asthma of the aged is not

denied but whether it is *solely* responsible for that asthma is seriously questioned

A word now about the treatment of chronic "intractable" asthma (not infrequently seen in the aged) with cortisone and ACTH Cortisone has brought as a rule only partial as well as transient relief to asthmatics In fact the hypoplasia of the adrenal cortex that follows the use of cortisone leaves the patient worse off than he was before And though ACTH has given complete relief for weeks or months the basic sensitivity to specific substances as demonstrable by skin test is not permanently set aside by ACTH and may cause a recurrence of asthma What is worse ACTH is itself a potent sensitizer if use of ACTH is discontinued and then after some weeks or months resumed the patient may be found highly allergic to it and may suffer a severe even a fatal reaction The use of ACTH in asthmatics should therefore be undertaken with full knowledge of its dangers and only after all other measures have failed

*Nervous System* —The aged are subject to many disorders of the nervous system mostly on a sclerotic and degenerative basis They call for no special attention here Only two organic conditions need be mentioned.

*Herpes zoster* is commoner in later than in middle years The point here to be stressed is the gravity of the condition not in its acute phase but in the residual pains that may last for months or even years and shorten by exhaustion the lives of persons previously robust and healthy Trigeminal involvements are especially trying Every effort should be made to give early and lasting relief if necessary nerve-block injections and necessary surgical procedures should be employed

*Paralysis agitans* is frequent progressive and distressing Because it is incurable it is also much neglected Yet much may at times be accomplished in alleviating its effects Various drugs may reduce the intensity of the tremor and should be tried singly and in combination They include strammonium belladonna barbiturates in small doses bromides and antihistamines Instruction in safety measures and in self help techniques should also be given the victims of paralysis agitans

*Functional nervous disorders* are common and of great importance in the aged Psychic and emotional stresses are frequent physical forces wane financial resources dwindle frustrations disappointments and tragedy are inevitable Hence functional troubles from simple psychoneuroses through psychosomatic pictures to the range of psychoses are met alone or in combination with various organic diseases

The physician must therefore be cautious in concluding either that the patient s troubles are wholly functional or that an existing organic lesion accounts for all his complaints

The mental capability of an aged person to enter into a contract financial marital or otherwise or to make a will has important medico-legal implications. The incompetence of children to assume such responsibility is recognized by law which has set age qualifications accordingly But no such limits are feasible for the aged although many reach the stage when they can no longer meet such responsibilities Under the law the aged are considered competent to the last unless legally proved otherwise

The aged are increasingly beset by difficulties and infirmities that make them less and less able to manage their affairs So they depend increasingly upon those about them children other relatives or strangers They tend to favor those on whom they depend and to be influenced by them in disposing of their possessions. Children as well as others may be devoted or neglectful altruistic or selfish So an old person often becomes the victim of designing sycophants (relatives or strangers) to the detriment of deserving members of the family or he quite competently decides to do more for kind strangers than for relatives who paid him no heed This leads to law suits in which the soundness of mind of the aged person at the time of action is questioned or the use of undue or improper influence upon him is alleged

Relatives must not only assume their responsibility toward their elders but realize that kindness is the best way to insure the good will of those elders and the protection

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the household Nor are members of the family unprejudiced or always reliable witnesses They too may exaggerate, minimize or hide information through sentiment or selfish design Every possible source of information should be used in cases that seem complicated or obscure

*Physical examination* and *laboratory aids* are therefore all the more important in arriving at a correct diagnosis in an aged patient

Our commonest mistakes are sins of omission failing to do what we should have done Most of them are included in *failure to make a regular and complete physical examination* A few examples of such sins are these taking the blood pressure in only one arm counting the pulse at the wrist not at the heart failing to count the respirations A patient was referred to the writer because of failure to respond to treatment for alleged Addison's disease The diagnosis was based on a blood pressure of 80/50 in the arm nearest the sphygmomanometer on the doctor s wall the hypotension was due to a vascular anomaly, the pressure in the other arm was 140/80 A rapid respiratory rate may point to pneumonia or circulatory trouble when other signs are minimal Temperatures measured in the mouth are useless in a dyspneic patient or one without teeth or with loose dentures or one that is loquacious or confused An unexplained anemia and leukocytosis in a hospitalized patient were finally traced to a large painless Vincent s ulcer under an upper plate

Failure to examine the genitalia and the rectum routinely is common in dealing with aged patients

The *laboratory* should be used more freely with the old to allow for the shortcomings of their medical histories and for the lesser symptoms of their organic diseases Of chief moment are routine blood count and urine analysis roentgenologic examination of chest digestive tract, skeleton and teeth determination of the blood s sugar and uric-acid levels Specialists especially the cystoscopist the proctoscopist and the bronchoscopist should be more commonly consulted about the aged patient than they are

## TREATMENT OF DISEASE IN THE AGED

Disease in the aged attacks old organs and tissues The objective of treatment therefore is to restore those structures to their current 'norm not to that of youth

*Medication* tends generally to be less effective in the old than in younger patients therefore not too much should be expected of it Since elimination of drugs is slower in the aged one must reckon with their *prolonged action* as well as their *cumulative effects* This calls for lower dosage This is especially true of opiates hypnotics, and even mild sedatives they should be given in smaller amounts lest their effect be prolonged beyond that which was intended The aged require smaller doses of digitalis This must be remembered in using powerful preparations like digitoxin since poisoning may follow a diuresis

Some drugs produce an *altered reaction* in the aged Hyoscyamine scopolamine and belladonna for example in addition to their usual effect at times induce delirium They should be used with caution and their effects noted, especially at night

The aged are prone to drink less of all fluids than do those in earlier years Hence special attention must be given to an *adequate water intake* by elderly patients receiving *sulfonamides*

*Vitamins* are more likely to be helpful than bitter tonics However the use of dilute hydrochloric acid (1 cc ) and pepsin (5 cc of essence of pepsin) frequently has gratifying results in those with achylia

*Cathartics* unless contraindicated by an existing lesion are preferable to enemas

*Surgery in the Aged* —Surgical treatment is yielding progressively better results in aged patients The record in fracture of the neck of the femur and that in prostatism are shining examples This improvement is due to a number of reasons—*better pre- and post-operative care better anesthesia better surgical technique* and *early ambulation*

The *most efficient therapeutic weapon* at the disposal of any physician in all phases of the care of the aged is sympathy The aged don t get too much of it at best A

of their possessions against predatory strangers When mental deterioration or other threat to capability arises there are proper legal steps which relatives can take to meet the situation

The physician has a frequent part to play in these matters He has the opportunity to study the aging person over the years and so can recognize early evidences of mental deterioration He also can learn much about the relations existing between that person and those about him If legal action ever arises, the physician is sure to be called to testify Therefore he should supplement *careful observation* of his aged patients with *carefully kept dated records*

*Surgical conditions* in the aged are not to be considered in detail in a medical text Their prevention however is an important function of the general practitioner in his care of the aging patient

*Hyperkeratosis* and *skin cancer* may be prevented by avoiding unnecessary exposure to sunlight Those with blond hair blue eyes, and a fair skin that blisters and peels instead of tanning should eschew sun worship, and should be increasingly careful as they grow older to avoid actinic rays including those of ' sun lamps

*Hernia* most often arises in youth or early maturity It should be surgically cured, not managed with a truss But all too often people wear a truss for many years As they grow older and gain or lose weight the old truss no longer fits Yet they refuse to change to a new one, but run increasing risk of strangulation, incarceration and other complications of hernia Those with trusses should be the most careful to avoid constipation Even in old age the best treatment for hernia is herniorrhaphy

*Cystocele rectocele, and uterine prolapse* should be repaired no later than the end of the child bearing period not only to insure better results but to prevent later cancer

*Gangrene* in extremities with poor circulation is better prevented by proper care of the feet than cured by mutilating surgical procedures On the other hand, in the presence of actual gangrene *amputation and return to some activity* are preferable in the old to indefinite hospitalization

*Accidents* are preventable Much needs to be done to safeguard the aged from injury by falling in their own homes The major hazards are throw rugs slippery stairs and floors loose toys articles left on a lower step to be ' carried up later' , long lamp and telephone cords stairs without proper banisters, and bathtubs and toilet seats without properly placed hand grips Night lights should be kept burning in home areas that the aged are likely to traverse at night

*Early ambulation* is especially important for the aged after operations injuries fractures and the like, to conserve strength and function and to prevent thrombosis and embolism

*Disorders of the organs of special sensation* are also outside the scope of this text Nevertheless, two of them are too important to be ignored in the most elementary discussion of the care of the aged *Presbyopia* is universal Everyone agrees that its correction is essential for the individual s safety as well as his functional capacity and happiness Nearly everyone is therefore willing to wear glasses and to have them checked and revised as needed But *deafness* which is extremely common and is even more of a handicap than defective vision certainly from the standpoint of happiness is all too often not corrected Moreover the physician doesn't advise a patient to select his glasses from the bargain counter of a department store neither should he send the deaf to a layman selling hearing aids The deaf should be sent to an otologist trained and equipped to select the proper device instruct the patient in its use, and counsel mastery of lip-reading

## DIAGNOSIS OF DISEASE IN THE AGED

The recognition of disease in the elderly has its peculiar problems

*History taking* is difficult The aged are forgetful and require detailed questioning Even so the information acquired is not always reliable The old often hide their symptoms if they are afraid that a confession of illness will jeopardize their employment At times the aged are guilty of malingering usually to gain sympathy but occasionally to inconvenience an unpopular member of

who by knowledge or experience may recognize their own portents (physicians, nurses, clergymen). He is too much concerned with the discomforts of the moment to realize that death is impending. Nor is it wise to tell him about it, except in the rare instances (homicide) in which an antemortem statement of legal import is at issue. In that case the law requires that the patient be informed of the probable imminence of his death and that he formulate his words in the light of that knowledge.

More frequent and in the aggregate more troublesome than pain are a number of lesser symptoms. Chief of these is thirst. In the dying it is complicated by the dry mouth and throat that make swallowing difficult or impossible. Minor degrees of breathlessness are frequent. Intensely annoying is the inability to cough up viscid secretions that accumulate in the trachea and pharynx. Failing strength prevents the patient from changing his position, with resultant distressing aches at pressure points.

Annoying, too, are the grief and hysteria of relatives unable to conceal their feelings. Zealous friends tax the patient with overlong visits and useless conversation. Whispering in the sickroom is more disturbing and disquieting than speaking in ordinary tones; what is not meant for the patient's ears should never be uttered in his presence.

The care of the dying, then, has several facets. The most important of these is nursing. A capable nurse who goes about her duties with quiet assurance sets the tone of the whole situation. In addition to the routine care required by any bed patient she must anticipate the needs which the patient is increasingly less able to express. Thirst is assuaged by frequent small sips of cool drinks—water, tart fruit juices, dry wine, carbonated water or champagne. Sordes and secretions in mouth and pharynx are removed with cotton-covered swabs dipped in glycerine. A suction apparatus can be very helpful. Frequent changes of position and shifting of supporting pillows relieve local discomforts. Cool sponging of the face and neck and the gentle use of a fan do much to relieve breathlessness and the sense of suffocation, and are not only more easily available but less annoying than an oxygen mask or tent. The nurse adjusts ventilation and illumination, keeping the light out of the patient's eyes—but drawing the shades only if there is photophobia—and keeping the temperature of the room cool. The weight of bed clothing may be lifted off the feet with a cradle, real or improvised. Woolen socks or stockings are more acceptable than heavy blankets. The use of electric light bulbs under a cradle is to be discouraged, but if tried should be most carefully watched and guarded because serious burns result at relatively low temperatures in legs with failing circulation.

The nurse can best control the attentions of the family and the visits of friends. A few old cronies, if welcome to the patient and if calm and cheerful in demeanor, may be permitted short stays at the bedside.

A special word is needed on behalf of the increasing numbers who die not at home or in a private room, but in the wards of hospitals. Hospital planning should include the provision of some degree of privacy for all patients: small wards (ten beds or fewer), semipartitions, the upper halves of glass and screenable, a nearby waiting room where relatives may sit out their vigil. A quiet room is useful for noisy patients or those requiring much attention, especially at night, and adds to the comfort and peace of mind of the other patients. It should not, however, be in direct view of or in communication with the main ward, lest it gain and hold an unsavory reputation in the minds of the rest of the patients. Transferring any patient to such a room for some casual reason in no way connected with an unfavorable prognosis may nevertheless arouse a sudden overwhelming fear of death in that patient. The writer remembers two such rooms that the ward patients knew as "Gates Ajar."

The role of the physician in the care of the dying has several aspects. His first concern is to shift the emphasis of treatment from curative to palliative measures. This does not mean the abandonment of all remedial procedures, but rather the avoidance of nuisance activities: operations that have nothing further to offer, needless tests, especially if they involve venipuncture

kindly approach, a patient ear for their troubles, and expressed appreciation of their problems, a cheerful word of reassurance and encouragement—these will often make the simplest remedies and procedures almost miraculously effective, absence of sympathy may render weak the most powerful measures that science affords

*The Care of the Dying* —This final task of the physician is well epitomized in the words of Worcester "Our duty to our patients ends only with their death and in the hours preceding there is much we can do for their comfort At the very least we can stand by them "

The physician should recognize the signs of impending death In a rapidly progressing illness these may appear with dramatic suddenness In a slow, wasting disease, their onset is often subtle and insidious They may therefore be overlooked or recognized too late by the physician for him to be of service in giving adequate warning to the family or to revise treatment in favor of comforting rather than curative measures

The family, or at least its responsible members need to be told that the patient is soon to die There are preparations to be made, relatives at a distance to be summoned, religious rites to be observed that make such warning necessary In the emergency, the physician may have to act for the family in summoning a clergyman of the patient s faith

But it is unwise to try to be too accurate in predicting the day and hour of death Such predictions often go wrong

There are various signs that warn of the approach of the end The most informative is the appearance of the face which Hippocrates describes in terms which have not been improved upon by his successors "A sharp nose, hollow eyes half open collapsed temples the ears cold contracted and their lobes turned out, the color of the whole face being green livid or lead-colored the lips relaxed pendant cold and blanched the mouth open cold sweats confined to the head, face and neck" And he further mentions the 'hands hunting through empty space, picking nap from the coverlet the hands and feet cold the belly and sides hot,' and the accumulation of secretions in the respiratory tract, when the "lungs discharge nothing, but are gorged with matters which boil as it were in the air passages Add to these the placidity of shock, with clouding consciousness shallow jerky breathing, a thin accelerating thready pulse that falls quickly away from the palpating finger a failing blood pressure a leaky skin and one has the full blown picture of impending dissolution Experience and an increasing knowledge of the prognosis in various diseases enable the physician to recognize the several features of this picture soon after their inception

Death comes oftenest at night, especially in the small hours after midnight when vital forces seem to be at their lowest ebb In the very old, death often takes over from his brother, sleep

Dying may be easy or hard, but in general it is easy It is easiest for those who die in sleep or suddenly It is easy in the deepening anesthetic coma that renal failure and acidosis induce at the end of the majority of diseases In most instances the severest suffering has usually ended hours or days before death Even in those whose last illness is commonly associated with severe pain as in coronary occlusion, there is often a complete remission of pain toward the end For example, a patient who had known the agonies of heart pain lived a whole day after the onset of his fatal coronary episode pulseless incapable of the least exertion, fully aware of his condition and its fatal outcome yet whispering of his great astonishment I have not the slightest discomfort

Death is hardest in a few rare conditions in which the mind is clear to the last while paralyses pain or convulsions predict and magnify the inevitable rabies tetanus strychnine poisoning acute ascending (Landry s) paralysis and a few others Equally distressing may be the suffocating dyspnea of a fast growing mediastinal tumor or status asthmaticus or acute bulbar poliomyelitis But such torments are less frequent in the aged than in those dying in earlier years

Fear of death itself is not often a major cause of distress for as a rule the patient is not aware that he will soon die (The commonest exceptions to this rule are those

it begins at birth and it ends at puberty, or at a convenient age (say 12 years) or when the patient is too tall to be put into a bed in the children's ward

But when does old age begin? At fifty, or sixty? There are those who are senile at forty, and others who are youthful at sixty five Or does old age begin with the involution of certain organs? Here again there is no definitive schedule ovarian function may cease in the thirties or late in the fifties The crystalline lens may lose much of its elasticity in the forties or not until the fifties or sixties The thymus atrophies in childhood Gray hair baldness, and the loss of teeth are not uncommon in the twenties yet the hair of the writer's father is not yet gray at ninety one The seeds of death are planted in us at our birth but the date of their fruition is unpredictable

But the chief reason that there will be few if any full time geriatricians is that no one admits that he is old until long after that fact is obvious to everyone else At a class reunion you note the doddering wreck that once was young John Doe and you congratulate yourself that you haven't slipped as he has Yet across the room John Doe is thinking the self same thoughts as he contemplates your state of decrepitude Each thinks the other a proper subject for a geriatrician's care but I go to a geriatrician I who am still barely middle aged? He who announces the limitation of his practice to geriatrics will probably starve

Every physician therefore must be a geriatrician in that the application of the principles of geriatrics must be part and parcel of his daily work Every physician must train himself to recognize in his patients the first evidences of old age He must look for the first signs of trouble in the apparently well for chronic diseases so often have their beginnings in the forties and fifties He must do what he can to retard the progress of aging and to mitigate and alleviate its effects *He should study* geriatrics while he is still young and has an objective point of view

REFERENCES


BARNES A R Anticoagulant Therapy in Cardiovascular Disease Proceedings of a Symposium on the Clinical Problems of Advancing Years Philadelphia Smith Kline and French Laboratories 1949

DRUCKER P F The Mirage of Pensions Harper's Magazine February 1950

DUBLIN L I Statistical and Social Implications in the Problem of our Aging Population Philadelphia University of Pennsylvania Press Publications of Bicentennial Conference 1940

HOYLE C Care of the Dying in Hutchison's Index of Treatment 13th Ed Baltimore The Williams & Wilkins Company 1947

KALLMANN F J and SANDER G Twin Studies on Aging and Longevity J of Heredity 1948 *39* 12 349

——— Twin Studies on Senescence Am J of Psychi 1949 *106* 29

KARSNER H J Involutionary Changes in the Cardiovascular System Philadelphia University of Pennsylvania Press Publications of Bicentennial Conference 1940

KERN R A El Cuidado de los Viejos Boletin de la Asoc Med de Puerto Rico 1942 *34* 117

——— The Treatment of Inoperable Malignancy Philadelphia Medicine 1950 *45* 1749

PEPPER O H P Notes in the Field of Geriatrics Med Clin N Amer 1936 *20* 127

——— The Principles of Diagnosis and Treatment of Disease in the Elderly Nebraska State Med J 1939 *24* 401

STIEGLITZ E J Geriatric Medicine The Care of the Aging and the Aged Philadelphia W B Saunders Company 1949

THEWLIS M W Geriatrics 3rd Ed St Louis C V Mosby Company 1941

TURNER G G Giant Gall Stone Impacted in Colon and Causing Acute Obstruction British J Surg 1932 *20* 26

WORCESTER A The Care of the Aged the Dying and the Dead 2nd Ed Springfield Ill Charles C Thomas 1940

drugs and modalities that can no longer be expected to produce benefits and only annoy the patient with painful pricks, injections, or uncomfortable positions But he should not fail to catheterize a distended bladder or tap a pleural effusion to ease the patient

The relief of pain is paramount Sedatives alone are rarely adequate if pain is severe Opiates should be used as needed, but it should be remembered that small doses are usually the most effective that morphine may be given under the tongue, and that crude preparations of opium administered orally may have a longer action than the alkaloids administered by injection Yet in severe pain morphine may give relief best when administered by intravenous drip (40 mg dissolved in 1000 cc of physiological saline solution and given at the rate of 100 cc an hour) Alcohol not only when taken orally, but even more so when given intravenously is helpful in relieving pain

The foods and fluids to be taken by mouth by the dying patient should be determined both in kind and amount by the patient s wishes and his ability to swallow When he no longer accepts these a judicious use of intravenous fluid may control thirst

The physician s visits brief but frequent should be calmly reassuring and reasonably cheerful Much the same principle should govern the demeanor of all who enter the sickroom The manner rather than the word conveys to the patient the comforting thought that he is not forsaken

Even when the patient is moribund the physician may be asked by the family for a consultation with another physician He should comply cheerfully and at once Early in his practice this writer upon receiving such a request from the wife of a patient two days before his death in the terminal uremia of chronic glomerulonephritis persuaded her against her will to drop the idea on the grounds that the outlook was hopeless and that such a consultation would involve a large fee and could do the patient no good Weeks later came a letter from the widow with this message You saved me a few dollars but you robbed me of the satisfaction that I might have cherished the rest of my life the thought that I had done everything possible for my husband in his last illness "

Should the physician ever speed the end and so reduce the patient s suffering? No Custom, tradition experience, social sanction, law and religion are unanimous in this and rightly so Euthanasia would be a long step backward in civilization Savages solved the problems of old age and chronic disease that way to use it now would be a return toward savagery It is a cherished axiom of the law of our civilization that a man is presumed innocent until proved guilty It is equally axiomatic in the practice of humane civilized medicine that a man is savable while he is still alive In these days of rapid advances in all branches of medicine next year next month tomorrow may bring the cure for the condition called hopeless today

But this does not mean that the physician should hesitate to give the normal dose of an opiate to relieve pain simply because there is danger that it might prove fatal to the patient in his weakened condition As strength ebbs, the margin between the therapeutic and the lethal dose grows ever narrower It is therefore to be expected that in some dying patient a proper dose of morphine given to control pain may induce a sleep from which he does not awaken With that contingency in mind the physician does well to summon a member of the family to see the patient before the opiate is given As to its possible effects the physician should be silent lest he be misunderstood

## GERIATRICS AND GERIATRICIANS

It is clear that a new specialty has arisen in medical practice the prevention and treatment of disease in the aged Will there be a new group of specialists geriatricians who limit their professional activities to this field? Ten years ago this writer did not believe so he is still of the same opinion

First of all it is impossible to define the limits of such a specialty for old age itself is not easily definable Those who would compare geriatrics to pediatrics forget that the domain of pediatrics is easily defined

it begins at birth and it ends at puberty, or at a convenient age (say 12 years), or when the patient is too tall to be put into a bed in the children s ward

But when does old age begin? At fifty or sixty? There are those who are senile at forty and others who are youthful at sixty-five Or does old age begin with the involution of certain organs? Here again, there is no definitive schedule ovarian function may cease in the thirties, or late in the fifties The crystalline lens may lose much of its elasticity in the forties or not until the fifties or sixties The thymus atrophies in childhood Gray hair baldness, and the loss of teeth are not uncommon in the twenties yet the hair of the writer s father is not yet gray at ninety one The seeds of death are planted in us at our birth but the date of their fruition is unpredictable

But the chief reason that there will be few if any full time geriatricians is that *no one admits that he is old until long after* that fact is obvious to everyone else At a class reunion you note the doddering wreck that once was young John Doe, and you congratulate yourself that you haven t slipped as he has Yet across the room John Doe is thinking the self same thoughts as he contemplates your state of decrepitude Each thinks the other a proper subject for a geriatrician s care but I go to a geriatrician I who am still barely middle aged? He who announces the limitation of his practice to geriatrics will probably starve

Every physician therefore must be a geriatrician in that the application of the principles of geriatrics must be part and parcel of his daily work Every physician must train himself to recognize in his patients the first evidences of old age He must look for the first signs of trouble in the apparently well for chronic diseases so often have their beginnings in the forties and fifties He must do what he can to retard the progress of aging and to mitigate and alleviate its effects He should study geriatrics while he is still young and has an objective point of view

REFERENCES


BARNES A R Anticoagulant Therapy in Cardiovascular Disease Proceedings of a Symposium on the Clinical Problems of Advancing Years Philadelphia Smith Kline and French Laboratories 1949

DRUCKER P F The Mirage of Pensions Harper s Magazine February 1950

DUBLIN L I Statistical and Social Implications in the Problem of our Aging Population Philadelphia University of Pennsylvania Press Publications of Bicentennial Conference 1940

HOYLE C Care of the Dying in Hutchison s Index of Treatment 13th Ed Baltimore The Williams & Wilkins Company 1947

KALLMANN F J and SANDER G Twin Studies on Aging and Longevity J of Heredity 1948 *39* 12 349

——— Twin Studies on Senescence Am J of Psych 1949 *106* 29

KARSNER H J Involutionary Changes in the Cardiovascular System Philadelphia University of Pennsylvania Press Publications of Bicentennial Conference 1940

KERN R A El Cuidado de los Viejos Boletin de la Asoc Med de Puerto Rico 1942 *34* 117

——— The Treatment of Inoperable Malignancy Philadelphia Medicine 1950 *45* 1749

PEPPER O H P Notes in the Field of Geriatrics Med Clin N Amer 1936 *20* 127

——— The Principles of Diagnosis and Treatment of Disease in the Elderly Nebraska State Med J 1939 *24* 401

STIEGLITZ E J Geriatric Medicine The Care of the Aging and the Aged Philadelphia W B Saunders Company 1949

THEWLIS M W Geriatrics 3rd Ed St Louis C V Mosby Company 1941

TURNER G G Giant Gall Stone Impacted in Colon and Causing Acute Obstruction British J Surg 1932 *20* 26

WORCESTER A The Care of the Aged the Dying and the Dead 2nd Ed Springfield Ill Charles C Thomas 1940

drugs and modalities that can no longer be expected to produce benefits and only annoy the patient with painful pricks, injections or uncomfortable positions But he should not fail to catheterize a distended bladder or tap a pleural effusion to ease the patient

The relief of pain is paramount Sedatives alone are rarely adequate if pain is severe Opiates should be used as needed but it should be remembered that small doses are usually the most effective, that morphine may be given under the tongue and that crude preparations of opium administered orally may have a longer action than the alkaloids administered by injection Yet in severe pain, morphine may give relief best when administered by intravenous drip (40 mg dissolved in 1000 cc of physiological saline solution and given at the rate of 100 cc an hour) Alcohol not only when taken orally but even more so when given intravenously is helpful in relieving pain

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ages that the extent of physical disability in this nation will progressively increase

One of our great medical needs today is provision for total treatment of chronically ill patients in terms of the everyday problems of living Many such patients cannot be sufficiently rehabilitated in self-care to live independent dignified and happy lives at home

The problem of providing an integrated service for the chronically ill is a complex one There is one aspect of the problem that stands out glaringly at present the need in our general hospitals for training programs to enable many of the so-called chronic invalids to live independently at home The hospital must assume great responsibility for prevention of disease definitive treatment of diseases and rehabilitation after disease

The modern concept of medical rehabilitation was developed during World War II The rehabilitation programs of the military services and the Veterans Administration demonstrated that planned integrated programs of convalescent care stressing activity as an adjunct to definitive treatment could reduce the period of hospitalization offset the deconditioning phenomena of bed rest and prevent the harmful psychological sequelæ which often result from extended hospitalization The techniques of physical rehabilitation and retraining for the severely handicapped developed by the military services also have profound implications for the even larger number of our civilian population who are disabled

The Hospital Council of Greater New York has recommended that bed requirements for rehabilitation and convalescent care be placed at one bed per thousand of population This would mean that approximately 20 per cent of the beds in general hospitals would be utilized for this purpose It was felt by the Council that the allocation of this number of beds and the introduction of a dynamic rehabilitation program would decrease hospital days provide facilities for the evaluation and training of convalescent and chronically ill and disabled patients and would help provide a program of total medical care

Medical examination x ray and the usual hospital routines are not enough to meet the problems of the disabled persons Such patients must be taught to use their residual abilities to the maximum Patients must be tested and then trained in the activities of daily living—in the simple things like turning over in bed dressing and undressing applying and removing braces getting from the bed to the wheel chair or the standing position These are everyday things but they are the foundation of self-care and physical independence

The practice of rehabilitation begins with the belief that the doctor s responsibility does not end when the acute illness is ended or surgery is completed it ends only when the patient is retrained to live and work with what is left This basic concept of the doctor s responsibility can be achieved only if rehabilitation is considered an integral part of medical service Any program of rehabilitation is only as sound as the basic medical service of which it is a part The diagnosis and prognosis must be accurate for it is on them that the feasibility of retraining is determined

In addition to the general diagnostic studies the medical evaluation of the orthopedically handicapped must include muscle tests determination of joint range of motion and tests for the inherent needs in daily living In the physical medicine and rehabilitation service at Bellevue Hospital a check list of ninety six items is used to determine these factors They include (1) bed activities such as moving from place to place in bed and the ability to sit erect (2) toilet activities (3) eating and drinking (4) the ability to dress and undress—tying shoe laces manipulating buttons zippers and other fasteners and applying and removing braces (5) hand activities—winding a watch striking a match and using various door knobs and latches (7) wheelchair activities—getting from the bed to the wheel chair the wheel chair to the bed and in and out of the bathtub and (8) elevation activities which include the needed abilities for walking climbing and traveling (Fig 229)

At first glance such a test list sounds formidable and time consuming but the necessary information may be easily ob-

# Chapter 30

# Medical Practice and Rehabilitation

By HOWARD A RUSK M D

TODAY, as medical science moves forward in the prevention and cure of infectious disease, chronic illness has become the nation s primary medical problem In 1900, seven chronic diseases (cancer diabetes intracranial lesions of vascular origin diseases of the heart diseases of the arteries cirrhosis of the liver and acute and chronic *nephritis*) *were responsible for 25 7 per cent* of all deaths in New York State Between 1900 and 1940, a period in which the population of New York State increased by 85 per cent and the total number of deaths increased by only 13 per cent the number of deaths from this group of chronic diseases increased by 200 per cent and now includes over two thirds of all deaths in the state

*One of the principal causes of the in*creasing prevalence of chronic disease has been the great advances in medical and surgical care which have prevented death and produced an aging population Two thousand years ago the average length of life was 25 years, at the turn of the century it was 49, today it is 67 2 In 1900 one person in twenty five was 65 years of age or older, it is estimated that in 1980 the ratio will be one in ten The chances are now two out of three that a young man now starting his working life at the age of 18 will live to his retirement age of 65 A 45-year-old man today has seventy in 100 chances of reaching the age of 65 and the chances for a 55 year old man are seventy eight in one hundred White men now at the age of 65 can expect to live an additional twelve and a half years on the average and white women an average of fourteen and a quarter years

What are the medical and public health implications of this increasing age level of the population? First as people become older their medical needs change and they demand more medical service In 1940 the 26 5 per cent of the nation s population over 45 required over *half the nation s* medical care By 1980 it is expected that the number of persons over 45 will constitute nearly half the population Today, we are busily studying and discussing the need and the best plan for increasing and distributing medical services yet the growing age level of the population indicates that by 1980 we may need nearly double the amount of *medical service that is available today*

Secondly lacking specific measures in the cure of many of the chronic diseases medicine must look to rehabilitation to teach those afflicted by chronic disability to live and to work as effectively as possible with what they have left Until medicine finds specific answers to the problems of the diseases of the heart and circulation rheumatic fever and arthritis cerebral palsy multiple sclerosis poliomyelitis and the other crippling diseases we must utilize the techniques of physical rehabilitation psychology social service and other allied specialties of rehabilitation to teach the disabled to live within the limits of their disabilities but to the hilt of their capabilities

Until we find the etiology and treatment for the chronic diseases producing disability we can expect as the population

INITIAL AND PROGRESS SUMMARIES

| |
|---|
| ACTIVITIES INHERENT IN DAILY LIVES |
| RANGE OF MOTION |
| MUSCLE TEST |
| PSYCHO SOCIAL |

FIG 229 (*Continued*)

trained by a therapist nurse a well trained volunteer or a member of the patient s family From special check sheets used for charting the activity accomplishments information is readily available both on the status of the patient at the time of admittance and on his progress while undergoing rehabilitation

The use of such a check list is particularly helpful if personnel are not available to do definitive muscle testing and accurate range of motion determination for the daily activities test can be completed in the hospital the physician s office or the patient s home The subsequent training program is designed to teach the patient the various skills and activities which he cannot perform

After the basic medical work up the physician in conference with other staff members prescribes a five-hour a-day program for the patient This program includes training in all the ambulation and elevation rooms and the remedial gymnasium occupational therapy physical therapy speech therapy and any other activity which may be helpful in meeting the specific needs of the patient

In a comprehensive rehabilitation program vocational guidance specialists should also be available to do guidance work and testing in order that the patient may be started on a prevocational exploratory and work testing program as soon as it is medically feasible However good basic rehabilitation can be carried out with the personnel available in the ordinary general hospital if such a program is properly organized supervised and prescribed by the physician

The rehabilitation of the hemiplegic person is a typical example There are a number of simple progressive procedures in the rehabilitation of the hemiplegic who suffers from one of the commonest disabilities seen in general practice In the early stages of treatment the following devices should be used to prevent deformities (1) footboard or posterior leg splint to prevent foot drop, (2) sandbags to prevent outward rotation of the affected leg (3) a pillow in the axilla to prevent adduction of the shoulder (Fig 230) Quadriceps setting should also be instituted to maintain muscle strength The procedure is relatively simple and requires no special equipment Its use however will prevent crippling anatomic deformities and hasten the rehabilitation of the patient

The next procedure indicated is the institution of pulley therapy This can be done simply with a small pulley attached to a goose-neck pipe over the head of the bed ordinary clothesline being used with a 1inch (2 5 cm ) webbing for the hand loop With

DEPARTMENT OF PHYSICAL MEDICINE & REHABILITATION — BELLEVUE HOSPITAL

NAME — DATE ADMITTED — CASE NO — WARD

DIAGNOSIS — AGE

ACTIVITIES INHERENT IN DAILY LIVING

| Non-walking Activities | Grade | Date | Walking Activities | Grade | Date |
|---|---|---|---|---|---|
| A 1 Roll to right left | | | H 1 Walk forward 30 feet | | |
| 2 Sit erect in bed | | | 2 Walk backward 10 feet | | |
| | | | 3 Walk sideward 10 feet | | |
| B 1 Comb or brush hair | | | 4 Open and close door | | |
| 2 Brush teeth | | | | | |
| 3 Shave or apply make-up | | | I 1 Open and close cylinder lock | | |
| 4 Wash extremities | | | 2 Open and close ice box door | | |
| 5 Manipulate bed pan | | | 3 Open and close drawers | | |
| | | | 4 Open and close padlock with key | | |
| C 1 Cut meat | | | 5 Open and close door hook | | |
| 2 Butter bread | | | 6 Open and close window | | |
| 3 Eat with fork | | | 7 Pull window shade | | |
| 4 Drink from glass | | | 8 Work light switches | | |
| 5 Stir coffee | | | 9 Push door bell | | |
| | | | 10 Work pull chain light | | |
| D 1 Dress | | | 11 Open and close cabinet lock | | |
| 2 Tie shoestrings | | | 12 Turn faucet | | |
| 3 Tie tie | | | 13 Open and close medicine chest | | |
| 4 Undress | | | 14 Open and close bottle | | |
| 5 Don braces | | | | | |
| 6 Remove braces | | | J 1 Up 15 degree ramp 3 feet | | |
| | | | 2 Down 15 degree ramp 3 feet | | |
| E 1 Write name and address | | | 3 Flight of stairs (1) handrail | | |
| 2 Fold letter seal envelope | | | 4 Flight of stairs no handrail | | |
| 3 Open envelope remove letter | | | 5 Up curb | | |
| 4 Open and close safety pin | | | 6 Down curb | | |
| 5 Use dial telephone | | | | | |
| 6 Turn pages of book | | | K 1 Cross standard street on green light—40 seconds | | |
| 7 Wind wrist watch | | | 2 Get in out of bus use turnstile—20 seconds | | |
| 8 Strike match | | | 3 Erect position to car | | |
| | | | 4 Car to erect position | | |
| F 1 Bed to wheel chair | | | 5 Pick up object from floor | | |
| 2 Wheel chair to bed | | | 6 Carry cafeteria tray with dishes | | |
| 3 Raise lower foot rests | | | | | |
| 4 Propel wheel chair | | | TOTAL NON WALKING (49) | | |
| 5 Open and close door | | | TOTAL WALKING (29) | | |
| 6 Wheel chair to chair | | | TOTAL ALL ACTIVITIES (78) | | |
| 7 Chair to wheel chair | | | | | |
| 8 Wheel chair to toilet | | | THERAPIST | | |
| 9 Toilet to wheel chair | | | | | |
| 10 Wheel chair to bathtub | | | | | |
| 11 Bathtub to wheel chair | | | | | |
| 12 Floor to wheel chair | | | | | |
| | | | | | |
| G 1 Bed to erect position | | | | | |
| 2 Erect position to bed | | | | | |
| 3 Wheel chair to erect position | | | | | |
| 4 Erect position to wheel chair | | | | | |
| 5 Chair to erect position | | | | | |
| 6 Erect position to chair | | | | | |
| 7 Erect position to toilet | | | | | |
| 8 Toilet to erect position | | | | | |
| 9 Down to floor | | | | | |
| 10 Up on floor | | | | | |

FIG 223

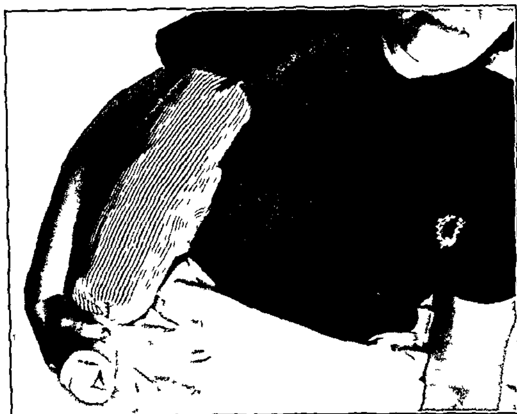


Fig 230 —A pillow placed in the axilla will prevent adduction of the shoulder

the stretching and passive exercise provided by pulley therapy the range of motion can be increased and adhesions prevented (Fig 231)

Pulley therapy has an advantage over the usual stretching exercises that are done passively for the patient knowing his own pain threshold will proceed to fully tolerated motion much more quickly Pulley therapy can also be used to aid in the reestablishment of reciprocal motion patterns

The patient at this stage should be encouraged to sit erect in order to reestablish balance Speech therapy if indicated should be instituted at this time In the absence of a trained speech therapist speech reeducation can be started under medical supervision by any teacher who has had some experience in this field In the case of aphasia it is well for the physician to point out to the patient and family the nature of the condition in order that the inability to use the tools of language may not be interpreted as loss or diminishing of the ability to think and reason

The next progressive stage in retraining the hemiplegic person is ambulation This should include (1) practice in balancing in the standing position and walking with the aid of parallel bars (2) learning a heel-and-toe gait to minimize clonus and reestablish normal walking habits *stressing reciprocal* motion and (3) using a short leg brace This last will be needed in approximately half the cases to correct foot drop (Fig 232) All the *equipment for training in ambulation* is simple and readily obtained by the general practitioner If parallel bars are not available two kitchen chairs may be used

*In the advanced stages* of retraining ambulation is continued with instruction in (1) crutch walking starting usually with the alternate four point gait and (2) elevation stressing climbing steps curbs stairs

RANGE OF MOTION

| JO NT | MOTION AND GE | | LEFT 45 60 90 1 5 | RIGHT 45 60 90 135 |
|---|---|---|---|---|
| SHOULDER | FLE IO E TENSION | A | | |
| | 0 180 | P | | |
| | ABDUCT ADDUCTION | | | |
| | 0 150 | P | | |
| | INT E T ROT TION | A | | |
| | 0 180 | P | | |
| ELBOW | LE ION EXTENSION | A | | |
| | 0 150 | P | | |
| | PRO T ON SUPIN | A | | |
| | 0 180 | P | | |
| W ST | DO S L L E FL | A | | |
| | 15 165 | P | | |
| | D LNAR FL | | | |
| | 60 1 0 | | | |
| H P | FLE ON EXTENSION | | | |
| | 0 12 | | | |
| | ABD CT DDUC ON | | | |
| | 0 5 | P | | |
| | INT T OTATION | A | | |
| | 5 13 | P | | |
| KNEE | FLE ON E TE S | | | |
| | 0 120 | | | |
| A LE | DO S L PLANTAR FL | A | | |
| | 5 105 | | | |
| | I E E SO | | | |
| | 60 120 | P | | |
| TOES | FLE ION E E S ON | A | | |
| | 60 165 | | | |
| | | | 5 60 90 135 | 5 60 90 13 |

| H D | MOT ON | | C T O 45 | MET CARPAL PHALAN E L 45 90 | P OX M L P GEAL 5 90 | T L P LA EAL 5 |
|---|---|---|---|---|---|---|
| LEFT | | | | | | |
| T UM | O OSIT O D | | | | | |
| | FLE E E S ON | P | | | | |
| 2 FI GER | FL O A D | | | | | |
| | EXTENS O | | | | | |
| 3 FI GE | FLE D | | | | | |
| | E TE ION | | | | | |
| 4 INGER | FLE O A D | | | | | |
| | EXTE SIO | | | | | |
| 5 FI GE | LEX O D | | | | | |
| | E TE S O | P | | | | |
| G T | | | | | | |
| T U B | O OST N D | | | | | |
| | FLE E E S O | | | | | |
| 2 FI R | LE O D | | | | | |
| | EX E | P | | | | |
| 3 FINGER | FLE O D | | | | | |
| | EX E S O | P | | | | |
| FI E | FLE O ND | | | | | |
| | E EN O | P | | | | |
| 5 FI GE | FL O A D | | | | | |
| | E TE N | P | | | | |
| | | | | 90 | 90 | 5 60 |

DATE__________________

THERAPIST______________

practice in many hospitals after an amputation above the knee to elevate the stump on a pillow. However, if such elevation is maintained for as long as two weeks, a flexion deformity will occur which will take from six to eight weeks of arduous, painful work before sufficient hyperextension can be regained for satisfactory walking.

In advising his patient on the selection of a prosthetic device the physician must be aware that not all limbs are suitable for all amputees. In fact, he must realize that not all amputees can wear artificial limbs profitably. A person in the older age group with an amputation above the knee cannot, as a rule, profitably be trained to use a prosthetic device if he is unable to perform a swing through gait on crutches.

The physician must point out objectively to the patient those skills which the patient can expect to achieve with proper training and those skills which the patient has little chance of ever regaining. Extreme caution must be taken as to the latter, however, as it is unwise to tell a patient what he can't do, for this cannot be determined in most cases until the patient has had adequate training. Training is absolutely essential if the amputee is to be successfully rehabilitated.

Because of the hopeless outlook in multiple sclerosis, therapy in general has been directed toward symptomatic relief and the approach has been a negative one. In rehabilitation the disability rather than the specific disease process which has produced it is our primary consideration. In multiple sclerosis, as in any other chronic progressive crippling disease, the problems are the same.

Retraining in the basic physical skills of daily living is primary; it is simply a matter of first things first, for daily activity skills are the basis for all subsequent rehabilitation processes.

It has been found difficult in many instances to differentiate between muscular inability due to disease and that due to atrophy of disuse. Sometimes only a test period of conditioning exercise will provide this information, which is vital in the training program.

It has been noted, especially in hand activities and gait training, that persons long incapacitated from multiple sclerosis will have alienation and overcompensation of certain muscle groups. With muscle reeducation and definitive therapeutic exercise, it is often possible to accomplish much correcting these conditions.

The psychiatric-psychologic problem must be approached by the psychiatrist, the social worker and the psychologist working as a team with the family as well as with the patient. After the patient's personality is thoroughly known by psychiatric examination, psychologic study and social service investigation, then each problem, as it comes up, can be handled with the full knowledge of the limitations of the patient, psychologically and physically.

Multiple sclerosis offers one of the most challenging problems in the entire field of rehabilitation, both from the physical and psychological standpoint. Therapy in this field requires patient training and deep understanding.

Emotional trauma may be present in any patient who has suffered a severe physical disability. The sudden shock and realization of the possible economic and social consequences of permanent disability frequently produce fear and anxiety which become as handicapping to the worker as the original physical disability.

When patients present themselves who are in need of psychiatric attention, it is the responsibility of the physician to recognize that need and see that proper referrals are made for such attention. In many instances where emotional problems are of a less severe nature, the general practitioner can resolve such problems. One of his greatest responsibilities with those patients who have severe physical disabilities is motivation—encouraging and convincing the patient that he can be rehabilitated. This motivation, to be most effective, must begin at the earliest possible moment following the accident or illness. The physician who knows something of rehabilitation can start at the time of the accident or crippling illness to allay the fears of his patient by giving him understanding, courage and hope predicated on an accurate knowledge of what



Fig 231 —Stretching and passive exercise provided by pulley therapy increase range of motion and prevent adhesions

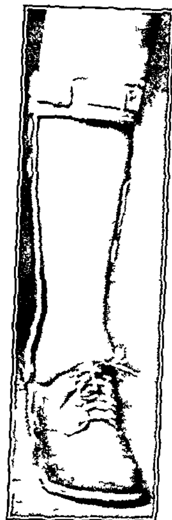


Fig 232 —A short leg brace is needed in approximately half of cases to prevent foot drop

and ramps Concurrently with the training in ambulation attention should be given to retraining in the activities of self-care and daily living

Obviously the physician himself cannot undertake the actual administration of the retraining but the therapist nurse volunteer or even a member of the patient's family can conduct the activities under the physician's supervision With such a program many of the complications usually following apoplexy can be avoided and a great deal of time and ability salvaged

Although the general practitioner is forced to call on the services of medical specialists when dealing with amputee patients, he must assume the responsibility for preparing his patient physically and psychologically for the amputation and for seeing that the patient has the proper prosthetic device adequately fitted and is trained in its use

One phase of the management of the amputee to which the physician should give particular attention is the immediate post operative period while the stump is being shrunken in preparation for a prosthetic device During this period of six or eight weeks the patient should be given graduated conditioning exercises in preparation both for crutch walking and for the later use of the artificial limb Measures should be taken to prevent anatomic deformities

For example it is not an uncommon

practice in many hospitals after an amputation above the knee to elevate the stump on a pillow However if such elevation is maintained for as long as two weeks a flexion deformity will occur which will take from six to eight weeks of arduous, painful work before sufficient hyperextension can be regained for satisfactory walking

In advising his patient on the selection of a prosthetic device the physician must be aware that not all limbs are suitable for all amputees In fact, he must realize that not all amputees can wear artificial limbs profitably A person in the older age group with an amputation above the knee cannot, as a rule profitably be trained to use a prosthetic device if he is unable to perform a swing through gait on crutches

The physician must point out objectively to the patient those skills which the patient can expect to achieve with proper training and those skills which the patient has little chance of ever regaining Extreme caution must be taken as to the latter however as it is unwise to tell a patient what he can t do for this cannot be determined in most cases until the patient has had adequate training Training is absolutely essential if the amputee is to be successfully rehabilitated

Because of the hopeless outlook in multiple sclerosis therapy in general has been directed toward symptomatic relief and the approach has been a negative one In rehabilitation the disability, rather than the specific disease process which has produced it is our primary consideration In multiple sclerosis as in any other chronic progressive crippling disease the problems are the same

Retraining in the basic physical skills of daily living is primary it is simply a matter of first things first for daily activity skills are the basis for all subsequent rehabilitation processes

It has been found difficult in many instances to differentiate between muscular inability due to disease and that due to atrophy of disuse Sometimes only a test period of conditioning exercise will provide this information which is vital in the training program

It has been noted especially in hand activities and gait training that persons long incapacitated from multiple sclerosis will have alienation and overcompensation of certain muscle groups With muscle reeducation and definitive therapeutic exercise, it is often possible to accomplish much correcting these conditions

The psychiatric psychologic problem must be approached by the psychiatrist the social worker and the psychologist working as a team with the family as well as with the patient After the patient's personality is thoroughly known by psychiatric examination psychologic study and social service investigation then each problem, as it comes up can be handled with the full knowledge of the limitations of the patient psychologically and physically

Multiple sclerosis offers one of the most challenging problems in the entire field of rehabilitation both from the physical and psychological standpoint Therapy in this field requires patient training and deep understanding

Emotional trauma may be present in any patient who has suffered a severe physical disability The sudden shock and realization of the possible economic and social consequences of permanent disability frequently produce fear and anxiety which become as handicapping to the worker as the original physical disability

When patients present themselves who are in need of psychiatric attention it is the responsibility of the physician to recognize that need and see that proper referrals are made for such attention In many instances where emotional problems are of a less severe nature, the general practitioner can resolve such problems One of his greatest responsibilities with those patients who have severe physical disabilities is motivation—encouraging and convincing the patient that he can be rehabilitated This motivation to be most effective must begin at the earliest possible moment following the accident or illness The physician who knows something of rehabilitation can start at the time of the accident or crippling illness to allay the fears of his patient by giving him understanding, courage and hope predicated on an accurate knowledge of what

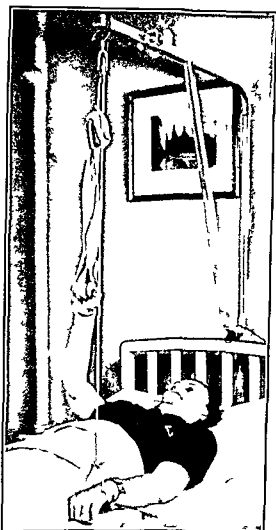


FIG 231 —Stretching and passive exercise provided by pulley therapy increase range of motion and prevent adhesions

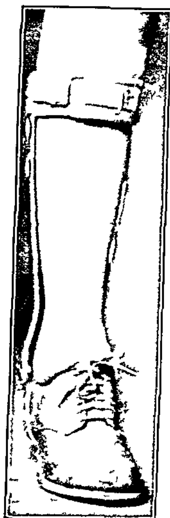


FIG 232 —A short leg brace is needed in approximately half of cases to prevent foot drop

and ramps Concurrently with the training in ambulation attention should be given to retraining in the activities of self-care and daily living

Obviously the physician himself cannot undertake the actual administration of the retraining but the therapist nurse volunteer or even a member of the patient's family can conduct the activities under the physician's supervision With such a program many of the complications usually following apoplexy can be avoided and a great deal of time and ability salvaged

Although the general practitioner is forced to call on the services of medical specialists when dealing with amputee patients, he must assume the responsibility for preparing his patient physically and psychologically for the amputation and for seeing that the patient has the proper prosthetic device adequately fitted and is trained in its use

One phase of the management of the amputee to which the physician should give particular attention is the immediate postoperative period while the stump is being shrunken in preparation for a prosthetic device During this period of six or eight weeks the patient should be given graduated conditioning exercises in preparation both for crutch walking and for the later use of the artificial limb Measures should be taken to prevent anatomic deformities

For example it is not an uncommon

# PART VII

# DISEASES OF THE NERVOUS SYSTEM

## Chapter 31

## Diseases and Abnormalities of the Mind Including the Neuroses[1]

By EDWARD A. STRECKER, M.D. and MANUEL M. PEARSON, M.D.

### THE PSYCHOSES

#### INTRODUCTION

THE mode of presentation of the diseases of the mind to the physician and the medical student has become somewhat formalized. The praiseworthy effort to attain completion often results in unduly lengthy discussions and fails to place proper emphasis on those conditions that are commonly encountered in practice. After all, while a description of paranoia makes fascinating reading, it is so rare that the physician may go through a lifetime of practice without meeting a single instance. Much more important is a thorough understanding and appreciation of schizophrenia, which is, perhaps, the most common psychosis, or paresis, which in its early stages is vulnerable to intelligent therapeutic attack. Multiple personality in hysteria provides material for engrossing speculation, but much more practical for the doctor is the knowledge of the common neuroses and their everyday manifestations. It is the opinion of the authors that *the neuroses and neurotic additions to organic disease constitute about 70 per cent of the practice of medicine*. Of overwhelming importance is the capacity to understand and to utilize therapeutically the fundamental fact that in every illness, no matter how purely *physical* it may seem to be in its manifestations, there is nevertheless an important *mental* component which must be thoroughly understood and energetically treated.

It is a grave mistake to isolate psychiatry. It is part and parcel of internal medicine. When one remembers that the human being is a *total organism*, with various physiologic and psychologic levels, and that the whole organism must always be studied in reference to the environment, it is easy to appreciate that so-called mental symptoms are often only manifestations of causes which in other instances or even in the identical patient may produce fever, alteration in the pulse rate and the like. Thus infection, fever, exhaustion, toxic agents like alcohol,

[1] The authors acknowledge the courtesy of being permitted to quote from Practical Clinical Psychiatry, Strecker, Ebaugh and Ewalt, 6th ed., P. Blakiston's Sons & Co., 1935 and 1940, and Fundamentals of Psychiatry, by Strecker, J. B. Lippincott Company, 1942.

can be done He can interpret to the patient the findings of the specialist in words that are understandable and meaningful He can explain to the patient the nature and extent of his disability, not in medical terms of the disability alone, but in terms of its effect on the vocational, social, economic family and personal life of the patient The physician must practice the art of medicine as well as the science

Regardless of the type of disability, the responsibility of the physician to his patient cannot end when the acute injury has been cared for It ends only when the physician has taken the responsibility for seeing that proper referral has been made to those agencies and institutions which are equipped to rehabilitate and retrain the patient with a residual physical disability

REFERENCES

1 NEW YORK STATE COMMISSION TO FORMULATE A LONG RANGE HEALTH PROGRAM Legislative Document No 69 Albany New York Williams Press 1947 p 42

2 Science Newsletter March 29 1948

3 Long Term Illnesses Seen as a Major Community Problem Requiring Extension of Medical Services Bulletin of the Hospital Council of Greater New York 1947 *3* 1

4 DEAVER GEORGE G and PETERSON KJELL J Pulley Exercises to Increase Joint Motion Archives of Physical Medicine January 1946

NOTE The photographs used are from a filmstrip REHABILITATION OF THE HEMIPLEGIC prepared by the Department of Physical Medicine and Rehabilitation New York University Bellevue Medical Center and distributed by FILMSTRIPS INCORPORATED, 140 West 86th Street New York City

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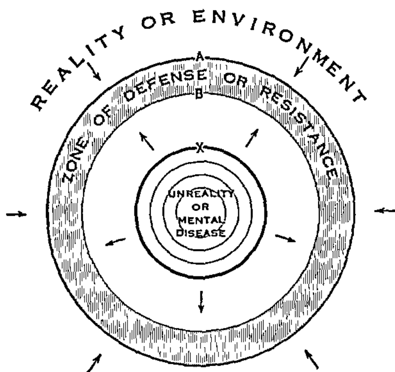



FIG 233

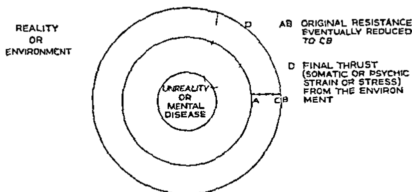



FIG 234

FIGS 233 and 234 —In figure 233 a normal amount of resistance against mental disease is indicated by the line A–B It is to be noted that this is in perfect contact with reality or environment at every point Unreality or mental disease and its various degrees of severity is indicated by the inner circles (From Clinical Psychiatry by Strecker and Ebaugh 5th edition Philadelphia P Blakiston s Son & Co 1940 )

measurable and concrete but probably they inflict more devastating mental damage Disappointment in love marital difficulties business reverses and many other situations cannot be observed in a test tube or viewed under a microscope but often they produce *anxiety* the effects of which may be observed as it saps the mental resistance and ends in mental disease

The recital of the causes of mental disease must not lead to narrow and restricted thinking Man presents various levels of functioning physical and mental These are distinguished by increasing complexity For instance at the lowest physical level there is the exercise of somewhat automatic functions like respiration at the higher levels one might consider voluntary motor activity

drugs, certain metals and gases, the more chronic intoxications like lues and tuberculosis, metabolic disease and arteriosclerotic disturbances or endocrine imbalances, all have mental components or symptoms which are really not separable from physical phenomena Conversely that whole group of experiences ordinarily called "emotional unquestionably influence the clinical pictures and even to some extent, the course and outcome of organic disease whether it be eczema or typhoid fever As a matter of fact, there is no dividing line between psychiatry and internal medicine Furthermore, unless there is penetrating study the symptoms of organic disease on the one hand and functional disease on the other, are often not distinguishable as to underlying causation For instance a patient with headache and projectile vomiting who barely escaped exploratory operation for brain tumor made a prompt recovery when the emotional conflict at the bottom of his symptoms was efficiently treated by psychotherapeutic measures The *current focussing* of attention upon psychosomatic medicine constitutes an acceptance of the principles of psychiatry In the area of psychomatic medicine there may be found numerous clinical proofs of fundamental psychiatric lessons That since man is a *total organism* somatic reactions are accompanied by appropriate emotional patterns and, *vice versa*, emotional experiences are at once reverberated in every tissue and cell of the body Finally, it has been demonstrated that too long continued disordered function due to unresolved emotional conflict eventuates in tissue pathology as in many instances of peptic ulcer (*See* Chapter 27)

### General Considerations

*Etiology*—In the consideration of the individual psychoses the causal and determining agents will be stressed, but at this point a broader and more philosophic view point may not be amiss In the final analysis mental disease and indeed all disease is due to the overthrowing of resistance Resistance against mental disease at any given point in the life history of an individual is determined by the sum total of his previous experiences (including ancestral assets and liabilities) and his reaction to them The vulnerability of this resistance is extremely variable not only from person to person but also it varies during the life cycle of the same individual, and finally, it differs according to the amount of the particular resistance which may be developed against this or that specific threat to mental stability

The resistance may be abruptly destroyed or it may be insidiously undermined Some simple diagrams may be illustrative (p 1407)

When the physician sees a patient who is mentally or nervously sick he is witnessing the end result of a serious disturbance of the normal relationship between that patient and his environment It is easy to understand how this balance representing normal mental health, may be upset not only by such physical agents as syphilis or arteriosclerosis of the brain but also by the factors ordinarily denominated emotional as *for instance* the stress and strain of prolonged fear or worry, or more remotely by lack of training during childhood so that problems of adult life cannot be met

More particularly the causes of mental diseases may be divided into those factors that are *predisposing* and those that are *exciting* The predisposing factors such as inheritance, critical age epochs like adolescence, the menopause or senility environmental factors such as defective childhood training occupation for instance contact with the various industrial poisons like white lead and a previous attack of mental disease favor the likelihood of the development of mental illness

The exciting causes actually *determine* the occurrence of the mental disease They may be chiefly physical or chiefly emotional The physical factors include fever toxicity of infection exhaustion exogenous intoxications such as may be due to alcohol drugs and the various industrial poisons the endogenous intoxications as, for instance in kidney liver or other disorders chronic toxicity notably due to lues metabolic disturbances endocrine dyscrasias and trauma

The emotional exciting causes are less

an psychoanalytic catharsis is a highly specialized technic that investigates the unconscious psyche (beyond the scope of the awareness of the patient) and through the interpretation of the everyday behavior, free association and the dream life seeks to give the patient enough self knowledge so that he may sever the bonds of restricting fixations become free of his symptoms and emotionally mature

### Classification

In psychiatry nosology faces even greater obstacles than it does in internal medicine The body of information from which a classification scheme must be built is creditably large but unfortunately it is not homogeneous For instance paresis in its etiology pathology and symptoms is as clearly understood as is typhoid fever or tuberculosis but on the other hand schizophrenia remains an unsolved riddle yet it must be fitted into any list of mental diseases

The accompanying grouping is based on a simple division into

(a) Organic
(b) Toxic
(c) Functional or psychogenic

Certain psychoses are predominantly organic that is they present pathologic alterations in the structure of the brain other psychoses are predominantly toxic in other words the symptoms are produced by bodily intoxication either by poisons introduced into the body from without (for instance alcohol), or by poisons created within the organism (uremia) finally in some psychoses the important factors seem to be functional or psychogenic

Naturally such a classification is far from conclusive As more knowledge is gained unquestionably there will be shifting from the organic to the toxic group and *vice versa* Even at this writing it is obvious that even in the most clear-cut organic psychosis (paresis) there are frequently toxic manifestations while as an aftermath of toxic reactions one often witnesses permanent structural alterations Furthermore the functional or psychogenic group as a whole will scarcely stand the test of time since even now many interesting organic and toxic manifestations have been recorded Finally the student must always remember that the prepsychotic personality of the individual may color deeply the expression of any psychosis

The psychoses that are starred will be described in some detail Wherever reliable statistics are available percentage frequency is given

*Examination and Symptoms* —The psychiatrist has no quick devices reliable short-cuts and but few instruments of precision at his command Master and student alike must utilize comprehensive and detailed history and conscientious examinations as a basis for sound and scientific opinion concerning diagnosis prognostic possibilities and treatment

The steps of history taking and physical examination cannot be given in detail The student will find adequate guides in any standard textbook [1]

Briefly the examination of the patient may be divided into the indirect examination or the history and the direct examination

It is particularly dangerous to neglect the *history* in psychiatry There are no instruments of precision by means of which the historical information may be discounted Unless the history is adequate important diagnostic clues will be lost For instance a record of lues suggests that the mental symptoms may be paretic of convulsions that the psychosis may be epileptic of recurring and transient blindness or deafness that it may be hysteria

The history may be conveniently divided into the account of the complaint of the present illness of the past history comprising the birth and developmental data the health record the school record the work record the sex development interests and habits and previous attacks of the personality and of the family

In psychiatric histories the history of sex is enormously important since there is scarcely a psychosis into which this elemental instinctive drive does not intrude

[1] The authors use the method outlined in Practical Clinical Psychiatry by Strecker Ebaugh and Ewalt 6th ed Philadelphia The Blakiston Co 1947

At the lower mental levels one witnesses the operation of the instinctive drives like self preservation and the physical sex urge, at the higher, there are ethical operations such as self-control or inhibition Though these various levels may be clearly recognized yet *even more important is the fundamental* fact that they are entwined into a *unit organism* In the instance of mental disease an exciting cause may enter at any level toxicity at a physical threshold as in pneumonia or anxiety at an ethical platform as in the case of a young officer in France who developed serious anxiety crises because he feared he might needlessly jeopardize the lives of his men as he led them into action In any event irrespective of the *level first involved the effect is to flood the* entire being and the individual is sick not only in mind and body, but in *all his mind and all his body*

Psychiatric thought tends more and more to the genetic dynamic approach The most clear-cut evolution in the study of mental disorder has been the recognition of the continuity of mental life in relationship not only to the organic growth of the individual but to the experiences which he undergoes and survives *A mental disorder* is to be studied from the earliest beginnings and as a stage to stage process The genetic dynamic approach so adequately formulated by Adolph Meyer does not regard the present difficulties and symptoms of the patient as the only or even the main objectives of study, but only one part of the large series of things which later must be studied from the earliest beginnings and dealt with as a whole

*Heredity* —Unquestionably inheritance is influential in the genesis of mental disease but its influence must not be overrated It should be remembered that in psychiatry, one must not expect Mendelian accuracy concerning heredity nor even that likelihood of transmission that attends such human defects as Huntington s chorea or family paralysis At the present stage of its development psychiatry will derive greater profit from the biometrician from clinical observation and from a study of environment than from a rigid interpretation of the inheritance factor

*Diagnosis and Prognosis* —To type a psychosis or neurosis according to certain diagnostic formulas and slavishly *to* prognose strictly according to the diagnostic label means little or nothing In no field of medicine is it more important to take into account the personal equation to consider first the patient and not be too much frightened *by the name of the psychosis* For instance schizophrenia may be hopelessly malignant, but in many instances a careful review of the life history may reveal many hopeful prognostic indications

*Treatment* —Under each psychosis the chief lines of therapeutic endeavor will be indicated, but there should be some brief mention of (*a*) prophylaxis and (*b*) psychotherapy

*Prevention* —Psychiatry abounds in opportunities for the institution of preventive measures Every patient should be viewed from this angle Never a case of paresis but that it should teach the importance of lessening the incidence of syphilis never an instance of schizophrenia but that its study should yield safeguards applicable to the training of children never a neurotic patient but whose life history should teach the prophylactic importance *of a better* contact between individual and environment

*Psychotherapy* —Psychotherapy is *not*, as popularly supposed a kind of mental sleight-of hand or miracle working that magically relieves patients *of symptoms* It is the important therapeutic weapon of the psychiatrist It is regrettable that it is not more generally employed in internal medicine Psychotherapy has very broad limitations It may be defined as an attempt to influence in the right direction the attitude of the patient that is to influence his attitude toward himself toward his mental *and physical processes and toward* his environment It is an effort to teach him to understand himself his illness and the cause or causes of his illness whether this cause or these causes lie in his body, in his environment or in the superficial or deeper layers of his mental life Persuasion suggestion useful habit formation self understanding strengthening of *morale are* all valuable psychotherapeutic methods Freud

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The history may be conveniently divided into the account of the complaint, of the present illness, of the past history comprising the birth and developmental data, the health record, the school record, the work record, the sex development, interests and habits and previous attacks, of the personality and of the family.

In psychiatric histories the history of sex is enormously important since there is scarcely a psychosis into which this elemental instinctive drive does not intrude

[1] The authors use the method outlined in Practical Clinical Psychiatry, by Strecker, Ebaugh and Ewalt, 6th ed., Philadelphia, The Blakiston Co., 1947.

A Organic Psychoses

| | | |
|---|---|---|
| 1 | Traumatic psychoses | 0 3 per cent |
| 2 | Senile psychoses | 12 1 per cent |
| *3 | Psychoses with cerebral arteriosclerosis | 6 4 per cent |
| *4 | General paralysis (paresis) | 10 6 per cent |
| 5 | Psychosis with cerebral syphilis | |
| 6 | Psychoses with Huntington s chorea | |
| 7 | Psychosis with brain tumor | |
| 8 | Psychoses with other brain or nervous diseases (Cerebral embolism paralysis agitans *meningitis tubercular* or other forms multiple sclerosis tabes dorsalis acute chorea encephalitis lethargica and other neurologic diseases ) | *1 2 per cent* (items 5–8) |
| *9 | Epileptic psychoses | 2 7 per cent |
| 10 | Psychoses with mental deficiency | 3 3 per cent |

B Toxic Psychoses

| | | |
|---|---|---|
| *11 | *Alcoholic psychoses* (This figure based on comparative admissions to the State hospitals in the United States in 1920 In 1922–1923 of 4444 consecutive admissions to the Psychopathic Wards of the Philadelphia Hospital 10 8 per cent had alcoholic psychoses ) | *2 2 per cent* |
| 12 | Psychoses due to drugs and other exogenous toxins | 1 1 per cent |
| 13 | Psychoses with pellagra | 0 37 per cent |
| 14 | Psychoses with other somatic diseases *(Including delirium with infectious disease postfectious psy*chosis exhaustion delirium delirium of unknown origin cardio renal disease diseases of the ductless glands epidemic encephalitis other diseases or conditions ) The percentage figure is undoubtedly too low It is based on admissions to public mental hospitals The majority of these psychoses are encountered in general hospitals in sanitoria and in private practice | 2 81 per cent |

C Functional (Psychogenic) Psychoses

| | | |
|---|---|---|
| *15 | Manic depressive psychoses | 16 0 per cent |
| *16 | Involutional melancholia | 3 2 per cent |
| 17 | Schizophrenia (dementia præcox) | 27 0 per cent |
| 18 | Paranoia or paranoid conditions | 2 8 per cent |
| *19 | Neuroses (This percentage figure gives no idea of the enormous frequency and importance of the neuroses It is based on the number of neurotic patients admitted to public mental hospitals which constitutes only a small fraction of the total ) | 2 1 per cent |
| 20 | Psychoses with psychopathic personality | |

The history should cover the first awareness of sex, how, when and with what preparedness and attitude evolution of the sex interest, and specific data on sex practice as noted in overt sex activity (physiologic data of erections, emissions or menstruation), as well as the more mental factors of sex fancies and dreams and their effects autoerotic homosexual and heterosexual features attitude to family formation The marital data should include date of marriage, marital adjustment with degree of satisfaction special gratifications and disappointments and difficulties pregnancies and their results attitude to the specific sex factors and satisfactions therefrom contraceptive methods reasons for the method used safety coefficient fear of pregnancy conflicts aroused by the practice

*Personality* —Human personality is so

dominant that its markings may be traced in the pattern of any psychosis, even in an out and out organic one like paresis. Personality in any individual at a given moment in his life is in one sense the condensed record of everything that has gone before in his life, his reaction thereto and the influence of his ancestral heritage. When it is remembered that the personality is made up of intelligence, instinctive drives, interests and hobbies, vocational aptitude and inaptitudes, mood, output of energy, social adaptability, *it will be seen at once how important* it is, how significantly it influences the expression of the psychoses and how carefully it must be considered.

The direct examination of the patient consists of the physical and mental examinations. They are scarcely separable, nor may the one be regarded as more important than the other. As a fair index of the truth and importance of this statement, we may cite again the clinical case of a man with intense headache and projectile vomiting, who barely escaped brain operation for want of a mental examination which when made readily disclosed that his symptoms were functional and not organic and due to an underlying emotional conflict. Conversely an error in diagnosis may easily follow the attempt to puzzle out the significance of somewhat atypical mental symptoms, the meaning of which is at once shown to be paresis if the blood and spinal fluid are carefully examined.

The physical examination consists of a general physical examination, the neurologic examination, the examination of the endocrine organs and the vegetative nervous system, laboratory examination and such contributory and special examinations as may be indicated. Without explanation it is obvious how diagnostically revealing are these examinations.

*Mental Examination*.—A mental examination is not difficult to make. A few suggestions might be helpful. (1) The examiner should not rush into questioning the patient, who should be encouraged to tell his story in his own way. (2) Friendly contact should be established with the patient. (3) Observations should be thorough. (4) Particular attention should be given to so called unco-operative phases of psychosis. (5) Throughout the examination, it should be constantly kept in mind that its purpose is not merely to record symptoms objectively but to interpret mechanisms that underly symptoms. (6) Record examination adequately.

The mental examination may be divided into the examinations of (1) General appearance and behavior, (2) stream of talk and activity, (3) mood (emotion, affect), (4) content and special preoccupations, (5) sensorium and intellectual resources, (6) insight, (7) special examinations.

While formal routine mental examinations are to be deplored, yet the examination when completed should reveal information covering all its divisions. Under each heading there will be found a list of symptoms and signs, some of which will be found in each case.

*I General Appearance and Behavior*.—Here, observation is the chief resource of the examiner. Without asking many questions he should note the general appearance of the patient, the facial expression, posture, the condition of the hair and clothes, the motor activity, whether it is quick or slow, purposeful and related to the environment or aimless and seemingly unrelated. Various important symptoms, including catalepsy, catatonia, cerea flexibilitas, compulsive and impulsive acts, distractibility, echopraxia, mannerisms, mutism, negativism, obsessional behavior, retardation, suggestibility, stupor.

*II Stream of Talk and Activity*.—This is the examination in a general way of the ever flowing stream of mental activity. There is indicated the speed and relations of the thought processes. Some of the following symptoms are likely to be observed: *Dissociation*, distractibility, echolalia, flight of ideas, garrulousness, incoherence, irrelevancy, mutism, neologistic formation, rambling, retarded speech, scattering, sound association, stereotypy, verbigeration, volubility.

*III Mood* (*Emotion, Affect*).—This is the most important part of the mental examination, since both in normal and abnormal mental life the stream of mental activity is given strength, direction and purpose by the emotions. An idea of the emotional reaction may be obtained from

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| 8 | Psychoses with other brain or nervous diseases (Cerebral embolism paralysis agitans meningitis tubercular or other forms multiple sclerosis tables dorsalis acute chorea encephalitis lethargica and other neurologic diseases ) | |
| *9 | Epileptic psychoses | 2 7 per cent |
| 10 | Psychoses with mental deficiency | 3 3 per cent |

B TOXIC PSYCHOSES

| | | |
|---|---|---|
| 11 | Alcoholic psychoses (This figure based on comparative admissions to the State hospitals in the United States in 1920 In 1922–1923 of 4444 consecutive admi sions to the Psychopathic Wards of the Philadelphia Hospital 10 8 per cent had alcoholic psychoses ) | 2 2 per cent |
| 12 | Psychoses due to drugs and other exogenous toxins | 1 1 per cent |
| 13 | Psychoses with pellagra | 0 37 per cent |
| *14 | Psychoses with other somatic diseases (Including delirium with infectious disease postfectious psychosis exhaustion delirium delirium of unknown origin cardio-renal disease diseases of the ductless glands epi demic encephalitis other diseases or conditions ) The percentage figure is undoubtedly too low It is based on admissions to public mental hospitals The majority of these psychoses are encountered in general hospitals in sanitoria and in private practice | 2 81 per cent |

C FUNCTIONAL (PSYCHOGENIC) PSYCHOSES

| | | |
|---|---|---|
| *15 | Manic depressive psychoses | 16 0 per cent |
| *16 | Involutional melancholia | 3 2 per cent |
| *17 | Schizophrenia (dementia præcox) | 27 0 per cent |
| 18 | Paranoia or paranoid conditions | 2 8 per cent |
| *19 | Neuroses (This percentage figure gives no idea of the enormous frequency and importance of the neuroses It is based on the number of neurotic patients admitted to public mental hospitals which constitutes only a small fraction of the total ) | 2 1 per cent |
| 20 | Psychoses with psychopathic personality | |

The history should cover the first awareness of sex, how, when and with what preparedness and attitude evolution of the sex interest and specific data on sex pace as noted in overt sex activity (physiologic data of erections, emissions or menstruation) as well as the more mental factors of sex fancies and dreams and their effects autoerotic, homosexual and heterosexual features, attitude to family formation The marital data should include date of marriage marital adjustment with degree of satisfaction special gratifications and disappointments and difficulties pregnancies and their results attitude to the specific sex factors and satisfactions therefrom contraceptive methods reasons for the method used safety coefficient fear of pregnancy conflicts aroused by the practice

*Personality* —Human personality is so

symptom variations influenced by the previous makeup of the patient yet the constant and dominant etiologic factor is the pathologic alteration in brain structure The symptoms are deteriorative and usually involve regression in the intellectual emotional and ethical fields In all these psychoses the patients are disoriented and reveal defects in memory attention and grasp In the functional psychoses on the other hand the sensorium is usually clear and the intelligence well preserved In the organic psychoses there are generally definite physical and neurologic signs the prognosis is poor but often the preventive opportunities are brilliant

## PARESIS

*Etiology* —The most notable example of an organic psychosis is paresis As is well known it is always due to invasion of the brain by the Treponema pallidum which may be demonstrated in the brain tissue

Only a relatively small proportion of luetics become paretic and therefore the nature of the secondary precipitating factor is an important and moot question On the one hand there must be considered a nervous strain of the specific organism on the other the effect of exogenous stress such as alcohol head trauma and indeed a whole group of damaging physical and emotional agents Since lues is more common in the male and also since it appears from ten to twenty years after the initial infection paresis is obviously more frequent in men It reaches its incidence peak in the fifth decade of life Juvenile paresis appears before the twentieth year (For detailed discussion of Paresis *see* p 1401)

## SENILE PSYCHOSIS

*Etiology* —Brain destruction conditioned by cerebral arteriosclerosis and other factors including old age and possibly by toxic and hereditarial influences The greatest incidence is between the ages of sixty and seventy five years Meggendorfer finds a familial tendency and believes that alcoholism favors early development

*Pathology* —Small brain narrow convolutions thick pia arachnoid fluid filled sulci tortuous and sclerotic vessels and microscopically ganglion cell loss and atrophy glial increase thick prominent vessels cortical fat excess and in the cortex and basal ganglia the presence of typical senile plaques

*Symptoms* —The student may advantageously regard the senile psychoses from three symptomatic angles The first is closely connected with the restrictions and limitations of old age Here we may expect irritability deterioration of normal emotional reactions obstinacy stubbornness self-centering of interests selfishness outbreaks of temper moral laxities or penuriousness The second is somewhat more closely connected with the brain pathology and embraces defects of orientation lessened mental capacity defective attention concentration and thinking a tendency to reminisce and fabricate and finally the keynote symptoms upon which the other phenomena are to a certain extent dependent namely *the failure of recent memory* Far less important in the clinical picture are the symptoms that are in some degree at least influenced by the personality Here we may consider the following subdivisions

(a) *Simple Deterioration* —Defective retention and memory reduced intellectual capacity narrowed interests Often there is suspiciousness irritability and restlessness usually nocturnal

(b) *Presbyophrenic Type* —Marked memory and retention defect with complete disorientation The patient is mentally alert attentive and able to grasp immediate impressions Forgetfulness leads to absurd contradictions and repetitions Prominent are suggestibility and fabrication

(c) *Delirious and Confused Types* —In the early stages there may be deep confusion or delirium

(d) *Depressed and Agitated Types* —Mental deterioration plus pronounced depression and persistent agitation

(e) *Paranoid Types* —Mental deterioration plus persecutory or expansive delusional trends

(f) *Presenile Type* (*Alzheimer s Disease*) —Profound dementia occurring as early as the fortieth year accompanied by aphasia apraxia and often an irritable or anxiou

close observation of the physical expression patterns and by questioning It is important to determine whether or not the emotional life is in keeping with the trend of thought

The psychotic patient may reverberate to any note in the emotional scale and here are listed only a few significant reactions euphoric exhilarated exhalted, depressed anxious, apprehensive suspicious perplexed irritable, furious, silly, indifferent dull apathetic

*II Content and Special Preoccupations* — In this division of the mental examination the examiner is concerned with the identification and study of such phenomena as illusions hallucinations delusions, autistic thinking obsessions, ideas of reference, symbolizations

*I Sensorium and Intellectual Resources* — The binding threads which maintain an appreciation of our relations in the environment to time place and person are readily loosened and even broken In fatigue, in sleep and in anesthesia in many mental disturbances acute mania profound depression in some of the organic reactions like the senile psychoses and, perhaps particularly in the toxic reactions like the deliria we may witness suspensions and even abolitions of conscious awareness of our temporal, spatial and personal connection with the environment The special symptom of inability to be aware of our environmental relations is called disorientation

Other mental functions tested under this heading are memory, remote intermediate and recent, retention and recall counting and calculation reading and recall writing attention school general and current knowledge

*II Insight* —The capacity of the patient to understand his psychosis and its symptoms It is important to record the degree and character of the insight

*III Special Examinations* —In given cases such special examinations as psychometric word association, hypnosis and dream analysis may be indicated

*Mental Mechanisms* —Psychiatry has passed beyond the descriptive phase This phase reached its culmination in Emil Kraepelin whose descriptive observations were so accurate that they have become classical But today just as the internist is not content with hearing a curious sound which signifies aortic regurgitation, unless he can understand the mechanics of the sound so likewise is the psychiatrist not satisfied with the knowledge of the fact that a patient has delusions or illusions, but he wants to know why in a given case the false beliefs or the sensory deceptions take this or that form

Interpretative psychiatry attempts to look beneath the surface of mental symptoms and discover their hidden meaning For instance why does a certain schizophrenic hallucinate so vividly and assert that every one is calling him a sexual pervert? Why does another patient stand for hours with arms outstretched in the form of a cross? What is there in the hidden mental lives of these two patients which has determined the shaping of their mental symptoms? In an hysterical amnesia what particular repressed experience is being concealed from conscious memory? In a psychasthenic fear let us say, of feathers is it the purpose of the phobia to keep from everyday thought an even more disagreeable and painful memory? And if so what is that memory? Is the given attack of acute mania during which the patient is markedly exhilarated and seemingly without a care in the world merely a pathologic compensation for conditions of life that the patient could no longer tolerate? The psychiatrist wishes to penetrate the concealed objective of these phenomena since the more he succeeds in unraveling their genesis the greater are his chances of helping the patient

## THE ORGANIC PSYCHOSES

1 General paralysis (paresis)
2 Senile psychoses
3 Psychoses with cerebral arteriosclerosis
4 Epileptic psychoses
5 Psychoses with mental deficiency
6 Psychoses with cerebral syphilis Huntington s chorea brain tumor encephalitis and other brain and nervous diseases
7 Traumatic psychoses

In this group there are a group of psychoses in which although there are wide

symptom variations influenced by the previous makeup of the patient yet the constant and dominant etiologic factor is the pathologic alteration in brain structure The symptoms are deteriorative and usually involve regression in the intellectual emotional and ethical fields In all these psychoses the patients are disoriented and reveal defects in memory attention and grasp In the functional psychoses on the other hand the sensorium is usually clear and the intelligence well preserved In the organic psychoses there are generally definite physical and neurologic signs the prognosis is poor but often the preventive opportunities are brilliant

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(*f*) *Presenile Type* (*Alzheimer s Disease*) — Profound dementia occurring as early as the fortieth year accompanied by aphasia apraxia and often an irritable or anxiou

depressive mood Pick's disease and other presenile deteriorations may occur

*Course and Prognosis* —There is apt to be a prodromal period of several months duration during which the patient is irritable, sleeps poorly, complains of malaise, muscular weakness and anorexia and becomes seclusive The patient wanders aimlessly about and may lose his way Then appear the typical defect and deterioration symptoms, involving all the intellectual, emotional and ethical faculties and notably the recent memory, the psychopathologic phenomena of old age and perhaps the type symptoms like presbyophrenia delirium and confusion depression and agitation or paranoid reactions

The signs of senility and physical decay are obvious

The course is essentially chronic and progressive and the outlook absolutely unfavorable

*Treatment* —Early recognition attains great importance in view of the fact that the senile dement is readily victimized by designing individuals and thus may bring disgrace to his family and waste his resources

The patient should be protected from the consequences of his psychotic behavior To be kept in mind are the liability of physical injury of sexual offenses or of disgraceful marriages Pyromanic proclivities or simply memory losses may result in serious burns and loss of property Suicide is frequent An easily digested diet warm clothing and measures against constipation must be provided Insomnia may be controlled by mild hydrotherapy and simple hypnotics Often a mental hospital is the wisest solution, not only for the patient but to relieve the distress of the family

## PSYCHOSES WITH CEREBRAL ARTERIOSCLEROSIS

Finer differentiations between senile and arteriosclerotic psychoses which may be demonstrated at the autopsy table and under the eyepiece of the microscope usually fall by the wayside when subjected to the cruder and more practical test of clinical practice Pathologically there are in the brain more areas of softening and not the typical finding of the senile brain—the senile plaque Arteriosclerotic psychoses tend to begin earlier in life Peripheral blood pressure helps little in differential diagnosis, it may be and often is low Perhaps in the arteriosclerotic psychoses attacks of irritability and violent anger are more frequent and severe than in pathologic senility A crude but fairly accurate clinical diagnostic guide is contained in the statement, 'Refrain from a diagnosis of arteriosclerotic brain disease unless there is evidence of general (headache, dizziness fainting attacks) or focal (aphasia, paralyses) brain damage ' (Strecker)

## EPILEPTIC PSYCHOSES

Epilepsy the historical and "sacred disease, ' is still a puzzle to science Even the very questionable diagnosis of idiopathic epilepsy is certainly not permissible unless the epilepsies of gross brain disease (paresis, cerebral lues), toxic and infectious epilepsies (uremia diabetes) and borderline condition epilepsies usually due to endocrine dysfunction are excluded Not only because of the undesirable associations that have gathered around the designation epilepsy but also because of the finer differentiations permitted by the extension of our knowledge, it is better to use the designation ' convulsive disorders " Electroencephalography, even in the present early stages of its development is definitely helpful in establishing the diagnosis and fairly typical brain wave graphs are obtained

Psychiatry is chiefly interested in the mental symptoms that occur in the course of epilepsy and in the personality of the epileptic

*Etiology and Pathology* —The actual cause of epilepsy probably revolves around those conditions which increase the sensitivity of the cortical platform to reaction The stock is usually badly tainted and Gowers states that 76 per cent occurs before the age of twenty years Various pathologic alterations in Ammon s horn in the Pacchionian bodies or edemas have been described (Lennox Cobb Winkleman) One also finds surface gliosis of the hemispheres syphilis arteriosclerosis, arrested develop-

ment and toxic manifestations The difficulty is that usually at autopsy the picture is clouded by the result of the repeated terrific onslaughts of the seizures upon the brain

*Mental Symptoms*.—There is scarcely a specific mental reaction in epilepsy and the diagnosis usually must wait upon the demonstration of the typical seizure or unquestioned petit mal Mentally the traditional irritability may assume such proportions that it is really psychotic, epileptic dream or twilight states with considerable confusion delirious confusion with an ecstatic hallucinatory delusional state or anxiety "conscious delirium" (epileptic fugue state) which has considerable medico legal import, since murder or sex crimes may be committed during the aimless journeys which the epileptic takes and of which he has not the slightest remembrance epileptic furor states following seizures during which the patient becomes maniacal homicidal destructive and a dangerous menace to those about him epileptic equivalent states in which a psychotic episode replaces the seizure, paranoid states in which the personality suspiciousness is carried to an extreme degree and finally, not only grand mal epilepsy but also petit mal may terminate in profound dementia in which every faculty of the mind is extinguished

While the epileptic may remain relatively normal mentally yet his *personality* is almost always pathologic One or more of the following traits are apt to appear Egotism conceit emotional instability hypochondriasis sickly sentimentality in religion inadaptability to environment, cruelty laziness irascibility impulsiveness excessive sexual tendencies criminalism violent impulses

*Course Prognosis and Treatment*.—Life is somewhat shortened not only as a direct result of the damage of the disease serious injuries status epilepticus secondary pneumonia but also the epileptic is apt to be a sickly individual with various gastro intestinal and skin disturbances The course is chronic and progressive The outlook is somewhat better in childhood

During the attack care should be exercised to protect the tongue teeth and body from injury In every instance the patient constitutes an individual therapeutic challenge Foci of infection should be removed rational surgical procedures should be carried out endocrine dysfunction combated lues and other systemic disease vigorously treated Practically in every patient it is necessary to prevent constipation bring the nutritional and functional activity of the body up to *par* and help to select a suitable, non dangerous and if possible out door occupation The drug of choice is dilantin $4\frac{1}{2}$ to 9 grains daily or if dilantin cannot be tolerated, phenobarbital 1 to 6 grains daily Other useful drugs are mesantoin (0 3 to 1 0 gm daily) mebaral or prominal (30 mgm to 0 2 gm three times daily), and for petit mal tridione (1 to 3 gm daily) With the appearance of definite mental symptoms the protection of a suitable institution should be sought for the patient Epileptics should be advised not to marry

## CONSTITUTIONAL PSYCHOPATHIC INFERIORITY

This is at best an unsatisfactory classification but nevertheless certain types of criminalism emotional instability, inadequate personality, paranoid personality pathologic lying and sexual psychopathy correspond rather closely to the conception which prompted the designation, constitutional psychopathic inferiority There is an obvious defect consisting of an apparent constitutional lack of responsiveness to the social demands of honesty or truthfulness or decency or consideration for others which incapacitates the patient from settling down to any permanent standardized activity The individual is therefore emotionally unstable is not to be depended upon, acts on impulses shows poor judgement and is constantly led into unwise activities the consequence of which he is able to realize intellectually but not evaluate Since one cannot explain or trace the abnormal behavior of these individuals to any definite disease or organic process the conclusion is justifiable at present that there is always some constitutional lack of endowment in each case and for purposes of classification the group is termed constitutional inferior

to which the word psychopathic is added to signify the marked instability and lack of the social responsiveness

The social and educational problems of this class of patients are of paramount importance The relationship of this group *to such problems* as prostitution venereal disease vagrancy delinquency illegitimacy alcoholism and drug addiction constitutes an active need for thorough research and the dissemination of knowledge throughout every community The need for careful supervision and definite measures to safeguard society at large from these individuals *should stimulate serious thinking by people* in general Kraepelin indicated the truth of this assertion when he showed that 54 per cent of the men and nearly one-third of the women in this group as a result of their moral deterioration come into contact with the courts on account of threats assaults quarrels and vagrancy

It is probably fair to say that constitutional psychopathic inferiority represents a kind of feeblemindedness which involves all spheres *save the intellectual one* that the inferior is like the low grade defective in that *he fails to profit by experience*

## THE TOXIC PSYCHOSES

Within the domain of the toxic psychoses is embraced a vast amount of clinical territory Much of this is directly included in the province of the general practice There is at once suggested a natural etiologic division *(a) into those* psychoses primarily due to the ingestion of toxic agents into the body as in the instances of alcohol and opium *(b)* those psychoses *influenced* by *autointoxications* within the body as in any infectious disease, or in even more direct intoxications like uremia in chronic infections *like* tuberculosis in such deficiency diseases as pellagra, in decompensating heart disease in the disturbances of metabolism occasioned by endocrine disorders In the last analysis *it is important to remember that every organic disease has its mental as well as its somatic components* Generally speaking the etiology of the toxic psychoses is usually clear whether it be on an exogenous or an endogenous basis the physical findings are those of the disease in question with a fairly constant background of fever leukocytosis and weight loss and in the skin kidneys *gastro intestinal tract,* and vasomotor and sympathetic systems, the usual accompaniments of fever or toxemia or both The prognosis is good

While the student must expect wide departure particularly in degree yet the mental paradigm of the toxic psychoses is *delirium* which in its pure expression includes clouding of the consciousness motor restlessness, hallucinosis apprehension and emotional instability

*Even more important than the therapy* of each individual toxic psychotic reaction are the highly important general principles of treatment (1) a large intake of fluid by mouth and if necessary subcutaneous colonic or intravenous administrations excepting in instances where there is brain edema (2) limitation of narcotics which are customarily used entirely too freely in the treatment of the toxic psychoses (in this connection it is suggested that the physician *have in mind the toxicity and the elimination* time of the hypnotic drugs he employs) (3) treatment of the usual accompanying constipation (4) hydrotherapy (5) *free* elimination (6) removal of poisons and infections including focal infection (7) dietetic and tonic treatment (8) protection of the patient against danger to himself and others

### Exogenous Toxic Psychoses

Obviously not all the mental *reactions* caused by poisons which may be deliberately *or accidentally taken into the body* can be described

The effect of *alcohol* which is unquestionably *toxic to the nervous system furnishes* a fair clinical example of the result of other serious poisons It is always narcotic it lessens motor activity increases *reflexes* diminishes physical strength lowers the fatigue point interferes with clarity of ideation impairs judgment and work capacity impairs memory and emotional stability and finally produces the debacle of complete intellectual emotional and ethical deterioration (*See* Chapter 12)

The student must not be too ready to diagnose alcoholic psychosis Alcoholism may be a symptom of paresis manic-depressive dementia praecox or epilepsy

*Opium* and its derivatives particularly *morphine* are frequently the resort of the psychopath when faced with even the low hurdles of life Their habitual use involves a profound deterioration of the ethics of the individual This is strongly marked in his efforts to obtain the drug

*Cocaine* is chiefly the drug of the underworld where it is often utilized by the criminal to pep up his courage for the commission of a crime and also to some extent it is dabbled in by a certain irresponsible stratum of so-called ' society The prolonged use of either morphine or cocaine as in the instance of alcohol finally deteriorates the taker to a low intellectual emotional and moral level

The efforts to combat cocaine addiction have been relatively successful and its incidence is now comparatively low On the other hand the use of an equally dangerous drug marihuana has increased

The symptoms of a psychosis with *Marihuana* vary depending upon the basic personality Agitation a loss of time relationships visual hallucinations of a sexual character and the complaints of ringing in the ears and dizziness are the most common ones Delusions of persecution ideas of reference flight of ideas and suicidal attempts constitute other features

The list of habit forming drugs is long and includes not only *ether chloroform cannabis indica* but even such milder hypnotics as the *bromides barbiturates* and many others

In the industries psychotic symptoms may be produced by *lead arsenic mercury* and the *gases* and many other industrial poisons (*See* Chapter 13)

### Special Treatment

In the toxic psychoses prophylaxis is almost unlimited Sensible explanatory scientific propaganda should lessen the incidence of psychotic reactions due to habit forming drugs protection and personal hygiene should make large inroads into the mental morbidity of the industrial poisons proper diet better control of infectious diseases and adequate periods of convalescence should reduce the mental pathology incident to metabolic disturbances and infectious diseases

The therapy of any exogenous toxic psychosis may be summed up under withdrawal free elimination hydrotherapy dietetic and reeducative measures Emergency methods in severe delirium tremens must be kept in mind (*See* Chapter 12)

## PSYCHOSES WITH SOMATIC DISEASE

Probably the largest field for psychiatry in the practice of medicine is in the psychotic reactions coincident with the fever and toxemia of infectious diseases with exhaustion with metabolic and deficiency diseases with cardiorenal disease and in short with every known pathologic condition There is no dividing line The patient with uncomplicated lobar pneumonia may in a few hours become delirious and consequently a problem in psychiatry The patient who is convalescing from influenza may suddenly become depressed and suicidal The patient with cardiac failure may rapidly become irritable suspicious confused and delusional Every somatic disease has clinically a mental as well as a physical expression which are interrelated

If the student keeps in mind the delirium paradigm—motor excitement incoherence hallucinosis disorientation deep confusion or at least some degree of clouding of consciousness then the psychiatric diagnostic problem becomes surprisingly simple Naturally variations in degree and departures will be encountered so that he may expect to find the framework of delirium filled in by such phenomena as convulsions catatonia stupor fear depression with suicidal attempts euphoria irritability suspiciousness delusional formation (usually transitory) dulness apathy coma or neurasthenic symptoms Likewise if the general therapeutic principles that have been stressed together with the specific therapy of the basic disease are kept in mind then the problems of treatment are usually not difficult and the results are highly gratifying

## MANIC-DEPRESSIVE PSYCHOSIS

*Definition*.—A recoverable but persistently recurrent type of mental disease second only to schizophrenia in importance and statistical frequency and marked by wide swings in mood and psychomotor reactions.

*Etiology*.—Unquestionably there are chemical, metabolic and organic factors at work in the genesis of this psychosis but they are still too little understood and too inconstant to be dignified into a specific etiologic role. Many years ago Kraepelin indicated the distortion of personality—the prepsychotic makeup—when he observed that among those who developed frank manic-depressive reactions, 12.1 per cent had manifested previously a depressive makeup, 9 per cent manic, 12.4 per cent were "irascible" and "nervous," 3 to 4 per cent, cyclothymic. More profitable etiologically than rigid neuropathologic interpretations is earnest attention to the "constitutional basis," which has its roots in heredity. This basis has physical as well as psychologic components and in its pure type we may think of an individual of the pyknic type, heavy, broad and thick set, who is an extrovert.

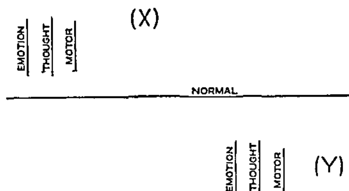



Fig. 235

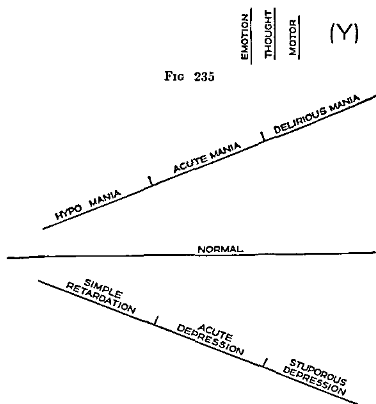



Fig. 236

Figs. 235 and 236.—Illustrating variations in the intensity of the symptoms in manic-depressive psychosis. ("Clinical Psychiatry," by Strecker and Ebaugh, courtesy of P. Blakiston's Son & Co., 1917.)

An extrovert is predominantly a man of action He "wastes" little time on reflective thinking accomplishes much routine work and is often effective and executive He expresses himself readily and positively Concerning questions issues policies beliefs he is apt to be very strongly *pro* or *con* but often his feelings are transitory His decisions are frequently of the "hair trigger" type He is a loyal enthusiastic friend and a bitter enemy but does not hold resentments for a long time and readily forgives He is energetic cheerful and sociable This type of personality does not necessarily spell manic-depressive but if the psychosis does occur it is often engrafted on similar dispositional traits

As precipitating causes one must consider psychogenic and somatic strain and stress and destructive influences traceable to faulty training and environment The psychosis is said to be more common among flight of ideas as evidenced by speech and also will be in a state of more or less marked physical or motor activity In acute melancholia the reverse is true This clinical point of view, usual parallelism between the unit symptoms and the chief degrees of severity of the psychosis is expressed in the following diagrams

There are numerous mixed states in which the unit symptoms referred to emotion, thought and motor activity are not in accord The chief forms are represented in the diagram opposite by the simple expedient of transposing the unit symptoms above and below a normal level line Thus maniacal stupor clinically consists of emotional exaltation slowing of thought and decreased motor activity

Since manic-depressive tends to recur throughout the life of the patient, one must expect many variations Only a few are given

| *Maniacal stupor* | *Agitated depression* | *Unproductive mania* | *Depressive mania* | *Depression with flight* | *Akinetic mania* | |
|---|---|---|---|---|---|---|
| E | I M | E M | M | I | E I | |
| I M | E | I | E I | E M | M | Normal |

females and is apt to be manifested before the twenty fifth year is more prevalent in urban than in rural areas and occurs with great freqeuncy in Jews and in Negroes

*Symptoms* —Waiving strict scientific accuracy for the sake of clarity, the student will probably get a workable conception of clinical manic depressive if he fixes his mind on the three functions which are chiefly affected—emotion (E), ideation (I), motor activity (M) — and pictures them either above or below a theoretical normal line according to the presenting phase of mania or depression Thus in classical or acute mania the emotions (affect mood) the ideation (activity of thought) and the motor behavior all present themselves to the observer as definitely increased or raised well above a normal average there being a more or less close agreement or parallelism between the individual unit symptoms Commonly the patient who is exhilarated or mercurial as to mood will likewise exhibit a corresponding degree of distractibility and

Viewed from an objective *psychologic* platform the patient in the manic phase of the psychosis is apparently without restraint and is seemingly unhampered by any counterbalance or inhibition in his emotional thought and motor expression the depressive seems bound in the chains of emotional depression thought and motor retardation This has led McDougal to regard the two contrasting phases of the diseases as the unchecked manifestation of the self-assertive and self submissive instincts respectively A more total point of view might consider the depressive phase as a temporary withdrawal in the face of defeat in the management of ego sex or (and) herd problems and the manic phase likewise a withdrawal and defeat which is psychologically camouflaged and prevented from reaching too clear a conscious realization by the unimpeded flow of energy in all directions emotionally ideationally and in the output of muscle energy Freud makes an analogy between depression and normal grief In normal

mourning the lost love object is identified in consciousness and thus the path is left open to a cessation of grief and the finding of new love attachments in pathologic depression the path in consciousness is blocked The psychoanalytic school explains depression with its guilt feelings on the basis of the lashing out of the super ego (the self-critique and ethical censor) against the defenseless ego

1 *General* —Disturbed sleep impaired nutrition (in mania) These symptoms are intensified in hyperacute mania, and fever with delirium like manifestations is often added Insomnia loss of weight coated tongue, sallow skin marked constipation (in depression)

2 *Body Systems* —Overactive heart, increased output of urine heightened metabolism (in mania) Cardiac activity weakened decreased urine output depressed metabolism Gastric achylia is not uncommon (in depression)

3 *Subjective Sensations* —Many varieties often associated with somatic delusions In depression there are complaints of numbness paresthesias dizziness ringing in ears

4 *Neurologic* —No constant findings but usually there are some disturbances In severe grades of mania there may be marked exaggeration of tendon reflexes and muscle tremor

TABLE 67

MENTAL

| *Manic* | *Depressed* |
|---|---|
| *Attitude and General Behavior* | |
| *Euphoria exhilaration* and *rapid shift* of emotional range (irritability impatience anger rage) to be noted in facies posture dress general behavior | *Depression* and *retardation* In mixed and stuporous reactions one may encounter various catatonic reactions (catalepsy cerea) |
| Stream of Mental Activity and Speech | |
| *Distractibility* volubility *flight of ideas* rhyming sound association | *Poverty of thought mutism* |
| Affect and Mood | |
| All degrees of *euphoria exhilaration* irritability *mercurial like alterations of mood* | Range from feelings of *inadequacy* and subjective lack of interest to *acute mental agony* Suicidal attempts Stupor |
| Mental Trend Content of Thought | |
| Inconstant shifting and often grandiose *delusions* | More tenacious *delusions* of wrong doing self accusation hypochondriacal somatic |
| Paranoid trends ideas of reference and influence persecutory delusions—all may occur | |
| Hallucinations rare but do occur in very severe manic states and in stuporous phases | |
| Illusions | Illusions |
| Sensorium Mental Grasp and Capacity | |
| Excepting briefly or in severe grades of excitement and depression the sensorium memory attention capacity orientation retention and recall counting and calculation reading and recall school general and current knowledge are not intrinsically disturbed The manic patient is apt to cover page after page with hurried lengthy untidy profusely capitalized underscored and crudely illustrated communications | |
| Insight | |
| During the attack especially in mania insight is at best quite faulty though rarely completely absent | |

*Mental and Physical Symptoms* —In listed form the sypmtoms are given in Table 67 the more prominent ones being italicized

*Physical Summary* —The absence of a specific pathognomonic syndrome does not imply that organic morbidity is insignificant or absent If the examination has been intensive and thorough *it will discover in the majority of instances somatic disturbances which at least indirectly are related to the psychosis* and which demand careful attention In addition the following phenomena have been reported by various observers

5 *Laboratory* —While there are no specific criteria there may be albuminuria and other pathologic urinary findings diminished or absent hydrochloric acid disturbances in blood chemistry A high basal metabolic rate has been repeatedly reported There may be a leukocytic increase in mania especially at the beginning of the phase in some cases a temperature and pulse rate rise during mania and again particularly in its inception a definite erythrocyte increase during the transition from normality to either excitement or depression and a fall under reverse conditions *i e* transition back to normality and blood pressure is higher both in mania and in melancholia than in quiescence

*Prognosis* —Manic phases seem to be somewhat more common than depressions Kraepelin stated that the first attack is a depression in 60 to 70 per cent of patients two-thirds of the melancholias are followed by remission and one third by mania and then a remission when mania is the first manifestation two thirds of the cases are likewise followed by remission Recovery from the single attack is the rule and the duration of the illness ranges from a few days to several months or longer Future attacks are often a repetition of the initial one although the tendency is toward greater frequency and severity The outlook seems to be better in proportion to the seriousness of the precipitating situation (so-called reactive types) the soundness of the heredity and the personality It is somewhat doubtful if any valid index of prognosis can be taken from the psychotic content though it has been stated that gross somatic and nihilistic delusions are unfavorable Mental deterioration is exceptional and may usually be explained by the addition of a complicating factor such as arteriosclerosis

*Treatment* – Given a strong constitutional basis sensible *preventive* measures should be set into motion early in childhood and proper training should be followed by some effort to modify the more destructive conditions of life In a large percentage of cases the attack itself must be dealt with in a suitable mental hospital or sanatorium From the somatic aspect each patient is a problem in internal medicine and any pathologic finding,—whether it be tuberculosis heart or kidney endocrine dysfunction gastrointestinal disturbance colonic stasis or *actual* foci of infection—must be dealt with unhesitatingly and intensively General measures of treatment are of the utmost importance The nutrition should be kept at the highest possible point and in some cases nasal feeding is unavoidable rest and often rest in bed particularly for depressed patients is helpful and hydrotherapy including the prolonged neutral bath is a valuable adjunct far superior to hypnotic overdrugging the patient should be protected against the well meant but usually harmful effect of many visitors With kindness sympathy tact and firmness the physician must manage the patient and attempt to direct his perverted energies into useful channels If the patient is at all accessible he should be frequently encouraged to talk things over with the physician

The greatest dangers inherent in the manic-depressive psychosis are suicide (stemming from the depressive phase) and exhaustion (stemming from the manic phase) The great advances in the treatment with convulsive therapy have therefore been truly lifesaving The treatment of choice for both phases is electroshock the best results occur in the depressed patient From nine to twelve convulsions of the grand mal type are usually required for the depressed patient but the manic patient requires fifteen to twenty In our experience the average patient may be expected to recover or improve from his depression within four weeks from the time convulsive shock therapy is started [1] There is no evidence to show that future attacks are prevented by electroshock therapy

Prolonged narcosis for as long as six weeks may be useful for some of the manic reactions the satisfactory drug being sodium amytal Sleep for from twenty to twenty-two hours a day is promoted by slowly increasing the dose of sodium amytal

[1] From Practical Clinical Psychiatry by Strecker Ebaugh and Ewalt 6th Edition Philadelphia The Blakiston Co 1947

mourning the lost love object is identified in consciousness and thus the path is left open to a cessation of grief and the finding of new love attachments in pathologic depression the path in consciousness is blocked The psychoanalytic school explains depression with its guilt feelings on the basis of the lashing out of the super-ego (the self-critique and ethical censor) against the defenseless ego

1 *General* —Disturbed sleep impaired nutrition (in mania) These symptoms are intensified in hyperacute mania and fever with delirium like manifestations is often added Insomnia loss of weight coated tongue, sallow skin, marked constipation (in depression)

2 *Body Systems* —Overactive heart increased output of urine, heightened metabolism (in mania) Cardiac activity weak

TABLE 67

MENTAL

| *Manic* | *Depressed* |
|---|---|
| Attitude and General Behavior | |
| *Euphoria exhilaration* and *rapid shift* of emotional range (irritability impatience anger rage) to be noted in facies posture dress general behavior | *Depression* and *retardation* In mixed and stuporous reactions one may encounter various catatonic reactions (catalepsy cerea) |
| Stream of Mental Activity and Speech | |
| *Distractibility* volubility *flight of ideas* rhyming sound association | *Poverty of thought mutism* |
| Affect and Mood | |
| All degrees of *euphoria exhilaration* irritability *mercurial like alterations of mood* | Range from feelings of *inadequacy* and subjective lack of interest to *acute mental agony* Suicidal attempts Stupor |
| Mental Trend Content of Thought | |
| Inconstant shifting and often grandiose *delusions* | More tenacious *delusions* of wrong doing self accusation hypochondriacal somatic |
| Paranoid trends ideas of reference and influence persecutory delusions—all may occur | |
| Hallucinations rare but do occur in very severe manic states and in stuporous phases | |
| Illusions | Illusions |
| Sensorium Mental Grasp and Capacity | |
| Excepting briefly or in severe grades of excitement and depression the sensorium memory attention capacity orientation retention and recall counting and calculation reading and recall school general and current knowledge are not intrinsically disturbed The manic patient is apt to cover page after page with hurried lengthy untidy profusely capitalized underscored and crudely illustrated communications | |
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ened decreased urine output depressed metabolism Gastric achylia is not uncommon (in depression)

3 *Subjective Sensations* —Many varieties often associated with somatic delusions In depression there are complaints of numbness paresthesias dizziness ringing in ears

4 *Neurologic* —No constant findings but usually there are some disturbances In severe grades of mania there may be marked exaggeration of tendon reflexes and muscle tremor

and it should include extra feedings preferably raw eggs and milk

Long rest periods are advisable Sometimes the prolonged bath induces quiet and sleep It is frequently necessary to employ hypnotic drugs in as small dosage as is possible Paraldehyde bromides and chloral veronal sodium amytal and other barbiturates have all been recommended

Always the patient is a problem in internal medicine Endocrine imbalances disturbances of circulation cardio-renal and gastro-intestinal pathology pelvic disease focal infection may all need vigorous treatment Constipation usually requires hygienic and dietary control massage and other measures Gynecologic consultations are needed not only to determine and treat pelvic pathology but also to obtain expert advice concerning endocrine therapy

In the vast majority of patients sanatorium or hospital care is imperative Infrequent visiting by relatives and friends should be the rule Experience shows they are likely to increase depression anxiety and apprehension

The patients are not always and certainly not throughout the entire course of the psychosis inaccessible to psychotherapeutic efforts Nonargumentative discussions persuasion reassurances suggestions are beneficial and certainly after the psychosis is over they are remembered with gratitude by the patient The nurse should be not merely an efficient robot but should work with the psychiatrist toward the accomplishment of the physical and psychologic adjustment

Occupational therapy is here as in the treatment of many psychoses the important therapeutic adjunct There is a wide range of choice—basketry weaving gardening and modelling

It may be valuable to change the form of occupation from time to time and it should not be so complex and intricate that it overfatigues the already wearied mind of the patient nor should it be so simple that it demands little or no attention and consequently provides no escape from the gloomy subject matter of the psychosis

After recovery the physician often aided by the social worker should supervise the patient and keep a watchful eye on the environment at least until the adjustment has been completed

## SCHIZOPHRENIA (DEMENTIA PRÆCOX)

*Etiology* —If manic-depressive is the psychosis of the extrovert then schizophrenia is strikingly the psychosis of the introvert The organic toxic and endocrine implications of præcox have been investigated by Nissl Mott Josephy Funfgeld Marcuse Kitabayashi Naito and others but thus far the findings while provocative are still too inconstant to justify the assumption of a specific causal relationship Perhaps our etiologic information is contained in the opening sentence of this paragraph

Schizophrenia tends to develop in persons with the shut in (Meyer) seclusive type of personality often on the basis of mental conflicts faulty habit formation and instinctive maladjustments particularly along the lines of sex extending back to early childhood and adolescence

The physical habitus in its pure form is the leptic or light relatively tall slender type The normal psychologic traits are those of the introvert

The introvert is the antithesis of the extrovert He is reserved a deep thinker disinclined to go into action Thought is his powerful weapon He is introspective and analytical At his best he plans thoughtfully for the future and often confers immense benefits upon his fellow men At his worst he is an impractical theorist visionary and dreamer To the world he appears to be distant gloomy cold unfriendly and lacking in strong personal feelings

The etiology of schizophrenia is so complex that in each individual patient there must be a careful evaluation of psychogenic toxic and organic (often endocrine) elements The psychosis frequently manifests itself early in life the largest percentage of cases appearing before the age of twenty five years It is more frequent in males than in females occurs earlier in males is more prevalent in cities than in rural districts is more common in the foreign population and more frequent in negroes than in whites

Prefrontal lobotomy has also been used by many authorities, including Freeman and Watts, though with better results in the chronically depressed and agitated patient than in the manic patient This procedure will be discussed more fully below

## REACTIVE DEPRESSIONS

A very healthy trend in modern psychiatry, thoroughly justified by increased information, is the separating out from the endogenous, constitutional and manic-depressive *depressions, the so called reactive* depressions Generally speaking, the reactive depressions are less dependent upon inner, constitutional factors and more dependent upon environmental circumstances Harrowes feels that the patient becomes depressed because of an etiologic life situation and continues to react to it in the psychosis The usual symptomatic picture is depression, lack of concentration and interest, loss of thought capacity increased *sense of effort, headache and forgetfulness*

The treatment is psychotherapy but since suicide is a real danger in these depressions, electroshock should be seriously considered

## INVOLUTIONAL MELANCHOLIA

Involutional melancholia is probably a mixed form of manic depressive in which the motor retardation is often replaced by restlessness and agitation It occurs more frequently in women than in men the ratio being about 3 to 2 it appears during the fourth and fifth decades of life or even later, heredity is said *to influence the development* of about 60 per cent of cases and the little understood organic and psychic pathology of the climacteric is probably also determining

The mood is depressed and apprehensive there is usually some degree of motor overactivity which may mount to a veritable frenzy of agitated excitement, suicidal attempts are common in about 10 per cent of patients there occur such catatonic phenomena as *fixed* attitudes, catalepsy negativism, stereotypy, grimacing, mannerisms, automatic movements, food refusal impulsive violence, resistiveness, destructiveness, violent scolding, unapproachability, *mutism, retention of urine and feces* often there is poverty of thought with monotonous and repetitive speech, the delusional formation is apt to be along the line of depression, self-accusation, self-depreciation, with hypochondriacal and gross somatic ideas

The organic morbidity is greater than in ordinary manic depressive and one may expect to encounter evidences of precocious senility, insomnia, profound disturbance of *nutrition with anorexia and sometimes* extreme weight loss circulatory, pelvic and digestive symptoms, particularly constipation and a great variety of subjective sensations

The course is quite protracted After a prodromal period of about a year the psychosis may endure for two, three, four or even more years

The prognosis is fairly good with a recovery rate of from 23 to 40 per cent *About 25 to 32 per cent are said to dement* About 20 per cent die within two years and the death-rate by suicide and intercurrent disease is fairly high The outlook is relatively unfavorable after the age of fifty five years or in the presence of advanced senile changes It is generally considered that a rapid gain in weight and general physical improvement constitute hopeful signs

*Treatment* —Every woman should be prepared for the menopause and the traditional ideas concerning its threat to the mind should be vigorously combated The physician should make a careful evaluation of the inherited organic psychic and environ*mental flaws in each patient* From such evaluation will come sensible preventive measures and safeguards

Should the actual psychosis develop suicide is such *a constant threat that tactful* vigilance must never be relaxed The best protection is the understanding and efficient psychiatric nurse

If no contraindications exist the most satisfactory treatment is electroshock therapy (*see* p 1427)

Frequently a gain in weight is the first sign of improvement and recovery The diet must be liberal rich in vitamin content,

statistics misleading. Of the early and mild group probably one fourth recover or at least attain a very satisfactory level of social readjustment. Of the more severe and outspoken symptomatically developed group 7.4 per cent recovered and 40.9 per cent improved definitely in five years or less. Catatonic cases are somewhat more favorable. The prognosis has been bettered by the introduction of the drastic therapies.

*Treatment.*—The social and economic threat of schizophrenia is both quantitatively and qualitatively so grave that every intelligent preventive measure should be instituted. These aspects offer the most brilliant opportunities particularly during the formative period of childhood. There is being delineated with more and more accuracy a personality pattern into which schizophrenia is so easily woven. This personality pattern has rather distinctive mental and even physical features so that it is not so difficult to identify. Children who manifest this type of personality should be made the target of intensive effort. Prevention should be carried out along the lines of attempting to modify this personality variously described as introverted, seclusive, schizoid. The prophylactic objective should be to strive for a more even balance between individual and environment and in some degree to "exteriorize" or socialize him.

For the child the home should be first and foremost a place in which is found an atmosphere of harmony and happiness. There should be neither unduly harsh discipline nor its opposite spoiling. Competition between brothers and sisters in the home for the favor of parents, particularly when spurred on by "playing favorites" by parents, is pernicious. The attempt to stimulate a child by too constantly pointing out the assets in brothers or sisters usually results in the production of inferiority feelings and is a hazardous process. There should be liberal doses of explanation to the child in the parent child relationship and particularly should punishment contain a generous leaven of explanation. Companionship with other children of both sexes, outdoor life, athletics and all reasonable socializing influences should be encouraged. It should be made easy for the child to bring his playmates into the home and there should be no risk that things would be seen or heard there that would shame him before other children. Sex and particularly the concrete facts of sex are always difficult for the potential schizophrenic and therefore effort should be made to prevent phantasy by supplying competent knowledge of sex hygiene and to discourage rumination by always discussing such matters without emotion and with only a modicum of moralization. Sex instruction should be begun comparatively early in childhood but naturally in a degree and in detail suitable to the age of the child.

Children have toward their parents an attitude of idealistic identification. Unconsciously they supplement their own weakness by identifying themselves in the parents. Here is a strong emotional bond leading to indiscriminate imitation and containing sources of danger particularly for the introverted child. The goal of any real psychology of childhood is to obtain for the child a true psychologic maturity. If this is not accomplished the child is destined for a life of slavish imitation of those who become the emotional surrogates for his parents. The parent-child bond must be loosened, not too abruptly but nevertheless surely, and independence of thought and action must be wisely and continuously encouraged.

Introverted children read a great deal and while their reading must not be too rigidly ordered, yet it should in some measure be directed toward types of literature not too luridly and completely phantastic. Religion supplies an important need and it should be a source of beauty and inspiration but social and practical too, and above all not grimly fear producing.

These are but a few of the conceptions that may be advantageously utilized in the attempt to prevent the development of schizophrenia not only in children but even later in life in those ingrowing personalities who are in danger of this chronic maladjustment.

From the standpoint of the treatment of the psychosis itself modern advances both in psychotherapy and pharmacology offer the patient a far better opportunity for

*Symptoms* —Psychologically, the foundation for the host of symptoms appears to be the withdrawal from reality and the dissociation between emotion (affect) and thought The withdrawal is manifested in many schizophrenic reactions and, perhaps, reaches its height in catatonic stupor during which the patient almost completely shuts himself off from contact with the environment Schizophrenia means splitting or dissociation and it too, is strikingly illustrated in many of the psychotic reactions of the patients in whom the emotional reaction apparently is at variance or very inadequate with the accessible content of thought On such a foundation there is erected an elaborate structure of clinical symptoms A summary based on a statistical study of many patients includes the following

1 *General Behavior* —Oddities of many types silliness incongruity stereotypy, mannerisms impulsive outbreaks untidiness marked mental inertia rigidity and attitudinizing

2 *Stream of Activity and Talk* —Autistic thinking dream like ideas feelings of being forced or of interference with the mind from the outside, physical and mythical influences incoherence rambling blocking evasiveness verbigeration, neologisms echolalia echopraxia mutism, negativism catatonia

3 *Mood and Special Preoccupation* —(a) Dissociation of affect inadequate and incoordinate affect ambivalence apathy indifference

(b) *Trend Reactions Topical Reactions Projection* —1 Persecutory ideas feeling of mistreatment food tampered with poisoned 'doped'

2 Ideas of reference—feeling of being talked about people pass remarks that "refer"

3 Ideas of influence — feeling of being hypnotized under mental control mental telepathy, mental spells hypodermic injections, radio machines

4 Hallucinations in various fields auditory hallucinations frequently of a religious pattern on the basis of overcompensation

5 Bizarre somatic sensations and delusions—organs have been removed brain has been removed vagina has been stopped up electric sensations through the body, electric wires connecting with the brain

6 Overcompensation in the form of day dreaming phantasies being God a saint leader of a new religion

7 Unintelligible and unexplainable activity

In the *paranoid* type (25 per cent) delusions particularly of persecution or grandeur, *often fairly well systematized* for a time at least and hallucinations are prominent in the *catatonic* type (10 per cent) there is negativism and conduct peculiarity *with phases of stupor or excitement* marked by impulsive queer, stereotyped behavior and hallucinations, in *hebephrenia* (52 per cent) there is silliness, unexplained smiling laughter grimacing mannerisms and peculiar and changeable ideas which have an absurd and grotesque content, and in the *simple* type *(8 per cent) interest is at a low* ebb there is apathy and strange behavior and delusions and hallucinations are either abortive and fragmentary or absent entirely

The field of *physical* symptomatology has been industriously tilled and although a specific picture cannot be traced many of the findings are strongly suggestive of underlying organic factors with an endocrine basis If such a basis exists it is probably most clearly expressed in the physical habitus described as leptic or asthenic The heart and vascular apparatus are often small Vasomotor sympathetic phenomena such as cyanosis localized sweating, edema, dilated pupils and increase in salivation are fairly common *Tuberculosis is rather* frequent In catatonic cases there is a tendency to show a low metabolic rate Gastro intestinal disturbances undernutrition and extreme constipation are often observed Kasanin reports high sustained sugar curve during stupor and Hertz finds shortening of the blood-coagulation time Somewhat remarkable are the occasional marked improvements following accidental and severe acute infections

*Prognosis* —Variability in diagnostic standards and the difficulty of obtaining accurate information concerning mild early and non institutionalized patients render

statistics misleading Of the early and mild group probably one fourth recover or at least attain a very satisfactory level of social readjustment Of the more severe and outspoken symptomatically developed group 7 4 per cent recovered and 40 9 per cent improved definitely in five years or less Catatonic cases are somewhat more favorable The prognosis has been bettered by the introduction of the drastic therapies

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marked improvement and even recovery than ever before

Insulin-hypoglycemic therapy is the treatment of choice in schizophrenia. The best results are obtained in cases of recent origin (under six months). Other somatic methods for schizophrenia include electroshock, combined insulin and electroshock, prolonged narcosis, electronarcosis, and prefrontal lobotomy.

The psychotherapy of schizophrenia is often fruitful when the patient is scrutinized in the long section of his life history according to the psychobiologic formula of Adolf Meyer. It brings to the fore such pertinent and therapeutically stimulating questions as "What are the resources of the patient? What has he to react with? What is the situation in life he is called on to meet? Can we modify his resources in order to enable him better to meet the situation or can we modify the situation so that he may better meet it with his resources?

There is much difference of opinion concerning the therapeutic application of psychoanalysis. Zilboorg advises so called "affective reintegration." It seems obvious that psychoanalysis must be modified if it is to be used in the treatment of schizophrenia.

The general management of the schizophrenic presents many interesting problems. The majority of well-established cases must be treated in mental hospitals or sanatoria but often a farm or ranch is helpful and in mild instances if there is good cooperation, patients may be treated in their homes. Whether the patient be in a hospital or at home, adequate nursing, occupational therapy and proper social service are important. The nurse is the representative of the psychiatrist and if well trained she will know how to attempt to check the inroads of phantasy and how to set forth in theory and practice the claims and advantages of reality. The social service worker if not too fanciful is valuable in the "follow up" of adjusted patients, and when patients are treated at home she should combat the danger of family disorganization. Occupational therapy is an extremely valuable and a necessary treatment adjunct. It is constantly symbolic of reality rather attractively garbed and it produces concrete fruits of effort rather than phantasy.

The good nurse will know how necessary it is to see that the patient has sufficient nourishment, that he is tube fed when necessary, that he is kept clean, bathed frequently, changed when he wets or soils himself, that dangerous and sharp objects with which the patient might mutilate himself or others are not available, that the patient has enough exercise, sunshine and fresh air, that the chronic patient is taught useful habits and some routine at least in the care of bodily functions, and the nurse, too, will minimize and control the physical dilapidation of appearance which is such an early result of the shutting out of reality. The prolonged bath and wet packs sometimes quiet the excited states. Apathy often must be the target of special measures: walks, calisthenics, physical culture apparatus, athletic games, indoor games, cards, other diversions, suitable motion pictures and the theatre, music, dancing, garden work, arts and crafts, especially weaving and basketry are all helpful. Sometimes in stupor visiting by relatives is beneficial.

## THE DRASTIC THERAPIES

The drastic therapies which are being continuously improved contribute a long needed weapon to the armamentarium of psychiatric therapy.

The chief drastic therapies are insulin shock, convulsive therapy, metrazol or machine induced, and the surgical operation of pre frontal leucotomy.

The use of insulin shock therapy is largely restricted to schizophrenia. The twenty-one to thirty five age group and the paranoid and catatonic types are the more favorable. The shorter the duration of the psychosis, the better the outlook. The prognostic indices are too loosely drawn and much treatment is given uselessly. Follow up studies made of schizophrenics ten years after insulin treatment indicate the real value of the treatment. Of 400 such patients treated in Swiss hospitals before 1937 59 per cent showed complete or social remission. Of a thousand cases treated in New York State hospitals 11.1 per cent re

covered, 26 5 per cent greatly improved and 26 per cent somewhat improved The corresponding figures for a control group of 1 000 untreated cases were 3 5 per cent, 11 2 per cent and 7 4 per cent

Contraindications to insulin shock therapy are cardiac arrhythmia due to organic disease of the conduction system, coronary disease severe myocarditis or valvular disease tuberculosis, organic impairment of the liver renal or pancreatic functions severe endocrine dysfunctions

Convulsive therapy induced by the electric machine has largely replaced metrazol, is extremely satisfactory and with intelligent selection of patients and skillful administration the danger is very slight It may be modified by curare It is very useful in manic-depressive, notably in involutional melancholia and in a considerable segment of schizophrenia

The contraindications are marked arteriosclerosis and hypertension pregnancy, marked bony changes either hyperplastic or degenerative seropositive syphilis tuberculosis, cachexia cardiovascular disease

The highest recovery rate in any large and varied group of cases initially diagnosed as schizophrenia will be achieved when insulin and convulsive therapy are skillfully combined in differing proportions in each case based on the actual symptomatology shown (Sargent and Slater )

The operation of pre frontal leucotomy has a limited but important application It has been used in involutional melancholia schizophrenia and a number of very severe anxiety neuroses and obsessive compulsive neuroses It is our feeling that criteria under which the operation was done in schizophrenia should be applied whenever the operation is contemplated

The main criteria are as follows (1) that the condition has been determined to be chronic and hopeless through clinical study (2) that all other methods of treatment have failed (3) that the operation does not entail undue risk *

It is extremely important that the use of the drastic therapies should not discount or minimize psychotherapeutic attention to the patient

## THE NEUROSES

In the consideration of the neuroses such an enormous clinical field is opened that it is extremely difficult to treat it briefly One may only acknowledge without discussion the enormous debt which modern psychiatry owes to Binet Janet Babinski Freud and the psychoanalytic school Adolf Meyer and many others

The neuroses may scarcely be considered even in brief presentation without some reference to psychopathology since the frequency of failure to diagnose and treat and above all to understand strikingly illustrate an outstanding and urgent need of a firm belief in the existence of a valid pathology which is not expressed in demonstrable structural damage There is a point beyond which physical diagnostic efforts and therapy may become harmful and even pernicious This is certainly so if they exclude a consideration of emotional factors if they are intensively and solely directed at the correction of minor and conjectural physical defects such as slight deviations of the nasal septum on the assumption that a minor operation will cure a psychoneurosis or finally if they are mistakenly focused on the physical expression of underlying emotional states

Psychotherapy in its modern sense presupposes the acceptance of at least a minimum of psychopathologic doctrine It is extremely difficult and hazardous to state what such a minimum implies Many of the signs and symptoms familiar to the organic neurologist for instance sensations have representations in the consciousness of his patient In a sense therefore, he studies minds the content of which the subjects are clearly aware and he studies and questions his patients chiefly from the standpoint of elucidating the findings obtained in his examination The psychiatrist

* Other psychosurgical procedures are trans orbital lobotomy topectomy thalamotomy and selective cortical undercutting They all are based on the assumption that those frontal lobe fibers which are connected with the ventral nucleus of the thalamus have to do with emotional overtones and that destroying these fibers will prevent anxiety of pathologic intensity Psychosurgery is still in the investigative stage and awaits final clinical evaluation —Editor

studies another mind, the content of which the patient does not clearly perceive, a not conscious mind, the investigation of which is profitable to the psychiatrist, since it contains a record of what has happened to the person during his lifetime (*See* Chapter 20)

*Classification* —The classification of the psychoneuroses is far from complete which is satisfactory enough for the present since it represents a state of flux awaiting additional knowledge Freud includes 'irritable weakness' or neurasthenia, anxiety states embracing anxiety neuroses' and 'anxiety hysteria', hysteria and obsessive and compulsive psychoneuroses Ross puts forward the suggestion that all neuroses represent faulty responses to difficulties In effect they constitute attempts to escape (1) By overreaction resulting in neurasthenia including the anxiety neuroses and anxiety hysterias of other writers (2) by underreaction or failure to react at all, resulting chiefly in conversion hysteria (3) pretending that the difficulty does not exist resulting in compulsion neuroses We shall employ a very simple classification hysteria, neurasthenia compulsion neuroses and anxiety neuroses

Naturally a real understanding of the neuroses must be derived from a study of underlying conflicts and mechanisms but a brief symptomatic list may be helpful

## HYSTERIA

*Somatic Symptoms – Sensory* Hyperesthesias hypoesthesias and anesthesias which are all non-explainable on any organic basis, narrowing of the visual fields photophobia, blindness hyperacousis deafness anosmia loss of taste headache *Motor* Paralyses of all varieties flaccid or spastic and sometimes with contracture Conclusive neurologic evidence of organic disease is wanting All types of abnormal movements—clonic choreiform, tremors—occur Pathologic attitudes and gaits may be displayed Every kind of vasomotor symptom may appear and muscular atrophy is not extremely uncommon The e manifestations are sometimes so striking that the French school of neurologists have attempted to differentiate such cases from true hysteria and have given them a separate grouping halfway between organic and functional disease, under the name of 'reflex paralyses' In addition to the symptoms which mimic usually in crude fashion every syndrome resulting from organic nerve irritation or defect, there may be exhibited many unusual phenomena such as rhythmical movements of various parts of the body head noddings, rotations and also bizarre attitudinizing The classical, full fledged convulsion is not usual though abortive and partial convulsive seizures are seen fairly often Perversion or loss of special function aphonia or mutism difficulty or inability of swallowing, globus vomiting amenorrhea, anuria, constipation or diarrhea may be a part of the symptom-complex

*Mental Symptoms* —*Amnesia* which is apparently a successful subconscious effort to keep something out of the field of consciousness It may extend for a considerable period before and beyond a particular incident or experience *Fugue* A span of time for which the patient is amnesic though during the fugue his actions are such that it seems to the observer that he must be conscious of his surroundings *Double personality* The fugue and the amnesic period probably have a content which is not acceptable to ordinary personal consciousness and therefore, there is acquired a kind of new consciousness constituting a second personality *Hallucination* It has been explained on the basis of partial failure in attempting to submerge a disagreeable complex the remnant remaining as an hallucination There may also be somnambulism hysterical fits deliriums, trances, stupor or dream states

## NEURASTHENIA

*General Symptoms* —*Fatigue* Often present on slight exertion and may be curiously selective in that it is chiefly manifested when the patient's interest is at low ebb Loss of weight Usually dependent on an appetite failure

*Local Symptoms* —*Alimentary* Capricious appetite anorexia, indigestion distention eructation nausea vomiting constipa

tion or diarrhea mucous colitis *Circulatory* Varying degrees of cardiac discomfort tachycardia palpitation pseudo-anginal sensations heart irregularity *Vasomotor* Pallor blushing sweating coldness, heat and numerous other phenomena *Genitourinary* Impotence nocturnal emissions genitourinary paresthesias dysmenorrhea dyspareunia frequency of micturition increased urinary output "loose kidney", *Respiratory system* Frequent "colds", shortness of breath sometimes hastened respiratory rate with shallow breathing *Nervous system* Peculiar sensations in head and in fact in every portion of the body feelings of swelling of scalp band around head bursting and stuffiness of head headache especially in occipital region peculiar uncomfortable or painful sensations in the abdomen rectum or breasts An almost universal complaint is backache Giddiness and dizziness are common and insomnia is rarely absent There may be photophobia musce volitantes and eye muscle fatigue ear noises intolerance of ordinary sounds *Mental symptoms* Inability to concentrate uncertain memory fear of insanity awkwardness and self consciousness in the presence of others feeling of inferiority irritability depression phobias anxieties

## COMPULSION NEUROSES

The clinical boundaries of the obsessive and compulsion neuroses are not clearly defined There is a group of symptoms including obsessions impulsions feelings of insufficiency nervous tension and anxiety Sometimes the obsessive thinking is ruminative consisting of preoccupations which "obsess" the mind but do not result in compulsive behavior However the step from obsessive thinking to obsessive behavior is natural and easy Obsessive acts symbolic of underlying trends are legion There are numerous ritualistic actions such as touching certain articles avoiding certain places and things food rituals or clothing rituals such as arranging clothes in exactly the same pattern after disrobing at night

## ANXIETY NEUROSIS

Anxiety neurosis or anxiety state a clinical type in which morbid anxiety or fear is the most prominent feature A general nervous irritability (or excitability) is regularly associated with the anxious expectation or dread In addition there are numerous physical symptoms which may be regarded as the bodily accompaniments of fear particularly cardiac and vasomotor disturbances the heart's action is increased often there is irregularity and palpitation there may be sweating nausea vomiting diarrhea suffocative feelings dizziness trembling shaking difficulty of locomotion Fluctuations occur in the intensity of the symptoms acute exacerbations constituting the "anxiety attack"

### Psychogenetic Considerations

The vast territory embraced by the neuroses is still too virginal to permit one to disregard a single possible determining factor Organic aspects a better evaluation of nerve fatigue endocrine influence all need additional rigid investigation In each patient there is demanded a carefully scrutinizing physical survey and treatment of the discovered pathology whether or not it be considered etiologic It is nevertheless true that at present at least psychologic investigation and therapy are more fruitful

Psychologically hysteria is resultant upon repression and subsequent conversion There is psychic trauma Painful ideas which for the particular individual are unacceptable to the conscious mind are not given an emotional outlet but are relegated or forced or *repressed* into the subconscious mind and become buried complexes The said painful ideas according to the Freudian school have invariably a sexual content Such repression often takes place during childhood Later these buried complexes are converted or rather the affect (emotion) with which they were associated is converted into a symbol which is objectively evident as an hysterical symptom

In a non Freudian sense an illustration may serve to clarify After a sharp action during World War I, a soldier was left

lying upon the field of battle. He feared to move because of the danger of an enemy sniper's bullet and for many hours he was compelled to remain rigidly quiet, surrounded by the dead and listening to the horrible cries and groans of dying. Later, he was led into an ambulance dressing-station totally deaf, although his hearing apparatus was physiologically intact. He was simply hysterically deaf and, furthermore he was amnesic. He remembered the action and could recall being brought to the ambulance dressing station but for the hours spent on the battlefield his mind was a complete blank.

What is the psychologic explanation? One may think of the horrors of war fatigue and exposure as directly causative of this hysteria. They were not. Even the emotion racking experience on the battlefield at most determined the time of the actual appearance of the hysteria. The dynamic mechanism, as always, was the conflict. In this instance, the conflict was between the instinct of self preservation and contrasting and opposed self and soldierly ideals. Self preservation triumphed, the conflict came to resolution and was converted into two disabling and protective symptoms—deafness and amnesia.

Hysteria is a large subject and only a few significant conceptions may be given. (1) Suggestion is an important factor. Babinski believed it alone served to explain hysteria. He felt that the symptoms were purely the result of suggestion and proposed for hysteria the designation 'pithiatism.' (2) The symptoms and signs of hysteria unlike those of neurasthenia, tend to be total such as deprivations of the special senses paralyses and anesthesias. (3) The hysteric views his symptoms objectively, is less conscious of his personal problems or conflicts and is less emotionally tense than for instance, the patient who has neurasthenia or an anxiety state. (4) Almost always the functional nature of the symptoms may be detected since they tend to exaggerate rather than simulate organic nerve or somatic disease, and there are many discrepancies in the clinical picture unexplainable on an organic basis. (5) Hysteria is a simple, naive, childlike device and its mechanism is usually not too difficult to penetrate.

*Neurasthenia* and some of the anxiety states, too are faulty responses—attempts to escape from the difficulties and conflicts of life. Freud stressed, as causative in neurasthenia, excessive masturbation in adult life and incompleteness of sex satisfaction. He stated that anxiety neuroses are more common in women and attributed them to coitus interruptus or ejaculatio præcox, in men to abstinence, frustrated sexual excitement coitus interruptus or senile conditions. Nonsexual stresses may be operative. The mechanism consists in a "deviation of the somatic sexual excitement from the psychic and in the abnormal utilization of this excitement."

The physician must be on the alert to detect the neurasthenic complex which may be a precursor or accompaniment of serious organic disease as for instance, in paresis or brain tumor. Furthermore, he must constantly remember that neurasthenia does not exclude the presence of organic disease.

Neurasthenia develops much more gradually than hysteria. The fatigue that is such a prominent symptom is not as is so often taught the cause of neurasthenia. It is effect rather than cause and is the aftermath of a long battle of emotional cross purposes. In the neurasthenic the circle of normal interests and activities rapidly diminishes and contracts so that eventually the attention is rigidly concentrated upon somatic sensations and reflexes such as the heart beat peristaltic movements of the stomach and intestines, muscle and joint movements. In neurasthenia these sensations and reflexes impinge upon the consciousness and are extensively elaborated while in normal health the individual is scarcely aware of their existence. It is true that in themselves they are unpleasant uncomfortable and even painful yet the center of psychologic attention has been shifted and the mind has escaped the even *more difficult and unpleasant facing* of problems and conflicts. Since the connection between the symptoms and the unsolved emotional problem is not open and direct in consciousness the psychopathologic mechanism employed saves the face of the

patient Not only is the ego spared the humiliation of self-criticism but social censure is avoided

Some of the symptoms encountered in the evolution of neurasthenia and the anxiety states have their analogies in the condition of a frightened animal let us say a cat frightened by a fierce dog The cat is in the grip of fear Physiologically the emotion acts by putting its body in the most efficient state for fight or flight The cat crouches, its skeletal muscles are tense, its hairs stand on end, the pupils are dilated there is a hissing noise the heart works rapidly the blood flows quickly and its pressure is increased breathing is quickened movements of the stomach and intestines are reduced to a minimum, and there are numerous and important ductless gland reactions

The human being is less often subjected to such acute and sthenic emotional crises but relatively the same effect is produced by less severe and more protracted emotional states resultant upon some serious life problem There may be apprehension anxiety worry shame, resentment and they as in the instance of the cat, are likewise expressed in the finely adjusted physical organism In the beginning the symptoms probably represent a fighting attempt to overcome the difficulty Eventually struggling and aggressiveness cease The individual is defeated He retires from the world of everyday normal distribution of interests and energies and engages in a close consideration of and an endless introspection into various residual sensations The typical neurasthenic patient with his great variety of subjective somatic complaints has now been produced

To illustrate let us picture a quarrel between husband and wife The subject of contention is the third member of the household the mother of the wife a querulous complaining and rather disturbing invalid to whom however the daughter is devoted For years husband and wife have quarreled about her presence in the home The husband wants her to leave The wife coaxes threatens gets into a violent temper weeps The husband goes to business The wife for the hundredth time feels herself driven into a corner Suddenly she is sick There is the sensation of an aching band about her head she is weak and tired her muscles are sore her heart seems to be racing along she is nauseated and faint She analyzes these sensations minutely What dreadful illness is threatening her? Heart disease? Actually she is organically sound The diagnosis is neurasthenia

In the background of this case there were many years of worry The conflict has been protracted and for this woman it has been very serious On the one side of the balance devotion to her mother and the dread of having her go to an institution on the other anxiety about her husband s love and the fear of losing him The conflict produced friction and fatigue The destructive emotional state began to be expressed by various physical sensations At first they were only occasional and insignificant manifestations Finally they became constant and alarming They demand consideration and treatment and a pathologic escape from an apparently unsolvable problem has been made unconsciously available

*Psychasthenia* which includes a large segment of the territory now occupied by the compulsion neuroses was regarded by Janet as a lowering of the psychologic tension , Meyer defines it as a lowering of general interest and tendency to rumination over what is accessible to the patient in his memory but is not squarely met and where the normal reaction is replaced by rumination substitution acts and panics Ross puts forward the suggestion that psychasthenia is a faulty response involving an effort to pretend that the conflict or difficulty does not exist

In any event psychasthenia apparently utilizes the psychologic mechanisms of displacement substitution and symbolism

As an example we may cite Ross interesting case of psychasthenia in a man who was obessed by a superstitious fear of the number 13 He remained in bed on the thirteenth day of the month hopped over each thirteenth step counted the syllables in conversations and felt a shock at the thirteenth or its multiples would not walk in Oxford Circus because of a sign Peter Robinson containing thirteen letters and

had numerous other disabling symptoms all associated with the number 13

*Modified analysis elicited that during* his boyhood there has been an ignorant superstitious serving maid in the home who had attempted sex relations with the boy Subsequently he had been sent to a boarding school and had lived for some years in a rigid religious atmosphere The disgusting experience of childhood had passed beyond the ken of conscious awareness The neurosis with the obsessive reaction to the number 13 had appeared in middle adult life

One may assume originally a conscious union between the idea of sex experience and the unhappy emotions (disgust fear shame remorse) called forth by the remembrance Soon the idea becomes too troublesome unpleasant and painful to be retained in consciousness where it must be constantly viewed By *means of the psychologic* mechanism of displacement the union is severed and the repugnant idea is dropped into the unconscious This leaves free and unattached the emotion from which the idea has been detached The emotion is then attached to a concept in itself innocuous in this case 13 Thus 13 becomes a substitute for and a symbol of the for gotten ' sex episode The second union is not altogether successful There is the tendency for the original idea to reappear and whenever there is any danger that it may break through into consciousness then there are manifested the frantic obsessive devices or symptoms related to the number 13

Frequently psychasthenia may be re*traced* to childhood experiences Not only sex experiences *can* be *dynamic* but anything that induced a vivid and strong emotional reaction that was never cleared up or explained and was finally repressed

The almost *uniform* occurrence of characteristic reactions in the history and clinical findings together with the favorable results of active treatment instituted at relatively late periods in the *course* of psychasthenia leads us to the conclusion that many psychoneurotic conditions might be prevented by early recognition and proper management The possible mental and emotional effects of diseases, accidents, operations and financial, sex and marital disturbances should be considered in the case of every patient consulting a physician

TREATMENT

General therapeutic indications are given since not only the particular neurosis, but the individuality of the patient and his *setting in life will often determine* modifications

Details of treatment which vary from patient to patient include hospital or rest house care rest in bed scientific nursing dietary control, massage hydrotherapy electrotherapy, occupational therapy supervision of the patient s activities, including visitors, correspondence reading graduated exercise tonic and in extreme conditions hypnotic medication There must be correction of any *actual* organic pathology

The principles of treatment for the neu*roses as developed at Stockbridge by Riggs* are as follows The patient is given an opportunity to tell his story in detail Next there is a thorough physical and mental examination followed by a frank discussion with the patient *concerning his* difficulties and the reasons for his maladaptation The patient is then informed of the plan of treatment and is given a daily schedule to meet his individual needs It consists of exercise, diversion and *rest* The keynote of the treatment is re-education It stresses the importance of dominating the emotions and of utilizing the intelligence to guide conduct Efficiency is emphasized The patient is impressed with the necessity of making clear cut decisions at first in trivial later in graver matters The *proper* use of the mind is described The harmful effects of worry unnecessary hurry inattention and self pity are elaborated They are manifestations of inefficiency The patient is instructed concerning rest which is not synonymous with sleep and is chiefly the temporary and volitional abandonment of responsibility

As a general guide toward rehabilitation the following steps are logical and helpful

1 *Establishment of Rapport Between the Physician and Patient* —This rapport to be effective must be based on a certain *amount* of respect and confidence on the part of the patient It is best furthered by a careful

investigatory program instituted by the physician at the first interview

2 *Aeration or Ventilation* — Aeration or ventilation of the conflict material presented by the patient may be carried out by means of Freudian catharsis by means of direct interviews by means of discovering and probing for such material from outside sources by hypnosis or by any other method The important thing is that the patient is given an opportunity to discharge and bring out in the open all of those life experiences which have been causing him serious concern either consciously or unconsciously

3 *Desensitization* —Desensitization is the procedure wherein the patient is required to face frankly the traumatic and unpleasant experiences of his past It is brought about in the first place by causing the patient to discuss at frequently repeated interviews the conflict material as elicited above These interviews are repeated until the patient can review these experiences without excessive emotional concern

4 *Re-education* —Re-education is carried out in connection with all of the above procedures It is essentially the development of clear insight on the part of the patient into the mechanism of his illness the establishment of new habits of response (as in desensitization) and the formulation by him of an adequate industrial social recreational and activity program to ensure future stabilization

5 In addition to the above it is often advisable to desensitize the patient s family to his illness and re-educate them into new habits of response toward the patient

6 All contributing physical factors are corrected as far as possible Measures for their correction are instituted at the earliest possible interview and are utilized as psychotherapeutic aids

## MILITARY NEUROPSYCHIATRIC DISABILITIES[1]

Neuropsychiatric disabilities because of their extremely high incidence are vital medico-military problems Not only are they extremely wasteful economically but much more than wounds they are disruptive of troop morale

Neuropsychiatric disabilities rarely appear with obvious diagnoses and there is a wide variety of symptoms and signs However the outstanding clinical segment is apt to be physical emotional or military misbehavior

A Physical ranging from convulsions coma lesser degrees of disturbances of consciousness paralyses deafness blindness severe headache, *etc*, to tics, limited anesthesias *etc*

B Emotional including depression often suicidal elation resentment irritability fear suspicion excitement, anger rage *etc* Admixtures are to be expected

C Military misbehavior embracing suspected fifth-column activities inciting to insubordination striking an officer drunkenness, neglect of duty grousing quarrelsomeness petty stealing *etc*

Unless the medical officer has some idea of the underlying nature of the emergency his treatment efforts are apt to be ineffectual or even harmful His examination should be extensive enough to answer the following questions Is it organic or functional? If organic is the seat of the disease outside the nervous system (uremic convulsions sinus headache *etc*)? If functional is it psychosis or psychoneurosis? If psychoneurosis is it the usual war neurosis conversion hysteria or a less frequent neurosis—neurasthenia anxiety obsessive-compulsive?[1] Can the disabling symptoms be speedily removed? Is it malingering?

The medical officer must not expect elaborate histories and in the field at best there will be available only a part of the information Reliable sources of information are the sick soldier s officers top sergeant and buddies

The medical officer s most reliable diagnostic instrument is careful observation However a brief neurologic examination (temperature pulse pupillary responses particularly to light tendon reflexes notably KJ abdominal and cremasteric reflexes

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[1] In World War II anxiety states were more common than conversion hysteria

Romberg's sign, posture, gait *etc*) may furnish valuable diagnostic and treatment leads of neurologic and psychiatric conditions, for instance, multiple sclerosis and paresis The psychoses of senility are excluded by military age limits However, there may be profound dementia due to alcoholism, epilepsy, brain tumors, presenile pathology, *etc*

Determined in practice by military exigencies, the major portion of the mental examination is dependent upon observation By observing carefully much may be noted General appearance state of body, clothing, facial expression attitude motor activity and whether it is purposeful or aimless, related to the environment or not, catalepsy, *stupor, mannerisms* negativism, suggestibility echopraxia, *etc*

If accessible, the soldier should be discriminatingly questioned in order to confirm impressions of observational data or to *determine the presence of decided mood* alterations, overactivity or underactivity of thought and speech, illusions hallucinations, obsessions ideas of reference, delusions, orientation memory including amnesia intelligence *etc*

An estimate of the emotional state and of consciousness is a necessary condition of diagnosis and treatment In manic depressive the emotional display is likely to be fairly clear-cut depressed often with self-blame and suicidal trends or exhilarated with quick shifts to other emotional reactions *in schizophrenia the emotional* expressions tend to be inadequate to the verbally expressed thinking or even at odds with it

Once conversion hysteria is well developed there is less emotional disturbance than would be anticipated in view of the dramatic character of the symptoms in the other neuroses there is *overconcern tension* and anxiety fear panic and so on

In a general way and in the absence of epilepsy paresis deep depression or grave neurologic or toxic pathology, disturbances of consciousness are prognostically good omens In the recoverab war neuroses particularly those occurring in combat, there is often an initial *befogged state* perhaps immediately determined by concussion fatigue, or food deprivation Even more favorable are acute psychoses with delirium dependent upon physical exhaustion They respond readily to simple treat *ment such as hot food increase of fluid in* take, rest, explanation

Malingering is a deliberately planned attempt to evade military duty or secure a discharge by feigning illness While not easy to detect, yet usually the simulation is overdone or incomplete with the absence of fundamental signs and symptoms Various technics like warming a clinical thermometer or taking purgative medicines or self inflicted wounds, may be employed Treatment should never omit giving the malingerer a "chance" Not infrequently detection, confession and frank *explanatory* discussion will convert him into a good soldier

Often military misbehavior is incipient evidence of psychosis, psychoneurosis, or *even organic neurologic disease Successful* treatment depends upon uncovering the underlying condition and dealing with it It is important to determine whether the behavior is consistently below army standards (indicating mental defect constitutional psychopathic inferiority) whether there was a rather abrupt change in the behavior pattern (indicating manic-depressive *schizo*phrenia paresis) whether there was a gradual alteration (indicating alcoholism anxiety neurosis) Was the conduct marked by overaction as in the boisterousness *aggressiveness and violence* of mania paresis or schizophrenic excitement or as more often in schizophrenia by underreaction as in the passive withdrawal *from* companionship and activities? The psychologic setting in which the misbehavior occurred may at once suggest corrective treatment For instance is the soldier *homesick? Is he worried* about bad news from his family? Perhaps he has had a gossipy letter hinting that his wife or his girl is interested in another man

The common war neurosis in World War I was conversion hysteria in World War II anxiety states were more usual In treatment particularly the medical officer *should* have a *working theory* of development There is an underlying unconscious conflict

The demands of the instinct of self preservation strongly activated by moving emotions fear horror and revulsion, versus ideals of soldierly duty patriotism honor training and discipline reactions Under conscious worry stress fatigue, or physical shock the conflict may be converted into protective symptoms, the clinical war neurosis

A few facts are valuable treatment guides (1) War conversion hysteria is more likely to occur in the intellectually average soldier neurasthenic anxiety and obsessive compulsive reactions in the superior soldier and officer (2) The symptoms of hysteria appear much more abruptly than in the other neuroses (3) Conversion symptoms—especially in combat—are apt to be total symptoms blindness paralyses hemi anesthesias in the other neuroses they are more often partial—blurring of vision weakness paresthesias (4) Often conversion symptoms may be removed by simple psychotherapy—such as suggestion (5) In war hysteria the earlier the treatment is instituted the better the prognosis[1]

(1) Early treatment was highly important, since often it was possible to remove symptoms by simple suggestion (2) The most satisfactory results were obtained in soldiers showing initial clouding of consciousness (3) The critical psychotherapeutic treatment time is when consciousness begins to clear (4) As soon as favorable secondary emotional trends begin to emerge they should be shaped and strengthened by positive and negative suggestion

Making due allowance for the occurrence of the disability in encampments or in combat and for the availability of psychiatric consultation and facilities treatment should utilize the following considerations

1 As soon as possible a brief examination and interview to determine the symptoms and to gauge roughly the soldier s personality

2 Establishment of rapport

3 An attempt to remove some of the symptoms by persuasion and suggestion

4 Desensitization and simple explanatory therapy

5 The production of positively and negatively conditioned psychic reflexes Positive concerning the advantages of returning to the front or in camp to the pleasant associations of the outfit Negative painting evacuation in gloomy colors (loss of the chance to participate in the honors of the outfit separation from buddies *etc*)

In a group of soldiers who have made fairly good symptomatic recoveries but who persistently retained a few symptoms the question of volitionally withheld co operation must be considered Without using undue severity and without trace of malice such men soon found that an invisible barrier had been erected between them and the other patients They were denied certain privileges and were assigned a reasonable amount of work such as policing grounds and digging latrines No one was permitted to impugn their motives directly yet they were confronted by a questioning expectant attitude Always the opportunity was afforded and indirectly encouraged, of talking things over always there was the invitation and temptation to change their status to a less dubious and happier one

Hypnotic medication probably paraldehyde and the barbiturates for severe insomnia, tincture of belladonna for tension benzedrine sulphate for depressions particularly with slow and difficult thinking and hypotension sodium amytal 0 3 to 0 6 gram intravenously when needed to secure relaxation or even mild hypnoidal states in order to remove inhibition so that traumatizing experiences are brought to the surface and ventilated and that the soldier is desensitized and may begin to build insight Narcosynthesis with the use of sodium pentothal may be used Occasionally hypnotism is helpful In the subsequent treatment of the war neuroses group psychotherapy is of considerable service

[1] These are highly important considerations notably during combat when time limits for restoration to duty (often only a few days) must be rigidly observed What is said of treatment in the combat zone applies with equal force to soldiers in encampments or in quiet sectors In the zone of active combat the neurosis will be much more severe at the onset the consciousness may often be clouded there will be fewer and poorer treatment facilities yet the results will be better than in encampments sometimes reaching more than 70 per cent restorations

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In a general way, and in the absence of epilepsy paresis deep depression or grave neurologic or toxic pathology, disturbances of consciousness are prognostically good omens In the recoverable war neuroses particularly those occurring in combat, there is often an initial befogged state, perhaps immediately determined by concussion fatigue, or food deprivation Even more favorable are acute psychoses with delirium dependent upon physical exhaustion They respond readily to simple treatment such as hot food, increase of fluid intake, rest explanation

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Often military misbehavior is incipient evidence of psychosis psychoneurosis, or even organic neurologic disease Successful treatment depends upon uncovering the underlying condition and dealing with it It is important to determine whether the behavior is consistently below army standards (indicating mental defect, constitutional psychopathic inferiority), whether there was a rather abrupt change in the behavior pattern (indicating manic depressive schizophrenia paresis) whether there was a gradual alteration (indicating alcoholism, anxiety neurosis) Was the conduct marked by overaction, as in the boisterousness aggressiveness and violence of mania paresis or schizophrenic excitement or, as more often in schizophrenia by underreaction as in the passive withdrawal from companionship and activities? The psychologic setting in which the misbehavior occurred may at once suggest corrective treatment For instance, is the soldier homesick? Is he worried about bad news from his family? Perhaps he has had a gossipy letter hinting that his wife or his girl is interested in another man

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# Chapter 32

# Organic Diseases of the Nervous System

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## INTRODUCTION

No branch of medicine requires so detailed a knowledge of the functioning of the entire body as does the study of nervous and mental diseases To be equipped properly to diagnose and treat nervous disorders one should have an adequate training in internal *medicine as well as a good knowledge of the* form and function of the nervous system The nervous system is a vital part of the total body economy not an isolated organ system Infections such as syphilis and tuberculosis vascular disease and tumors all affect the nervous system at times just as they affect other parts of the body and a full understanding of these factors requires some knowledge of their effect on the other parts of the body

The physician or student should train himself to make as accurate a diagnosis as possible by careful observation of the patient s signs and symptoms and their correct interpretation in light of his knowledge of the structure function and pathology of the nervous system In some cases determination of the exact diagnosis may be impossible without detailed laboratory and other special studies such as encephalography but recourse to such studies without prior careful observation and correct reasoning leads only to a machine made diagnosis much to be deprecated

The *history* in a nervous case is often of more importance than a good examination It should be taken carefully, in chronologic order and, as far as possible in the patient's own words Sometimes the patient will have to be directed in this story but an effort should be made not to ask leading questions This is more important when one is dealing with a functional rather than an organic case An idea of the patient s past life his heredity his mode of living his recreations and vices if any is important As the case unravels itself questions will suggest themselves to the examiner For example a complaint of pain should always be elaborated upon particularly its location its reference if any its character the presence of anything which aggravates it such as moving or coughing the time of day it occurs and if present at night whether it prevents sleep or awakens the individual Functions of the sphincters especially that of the bladder should be carefully inquired into Difficulties in the control of the urine which make their first appearance after the age of fifteen or twenty years will quite often have to do with involvement of the central nervous system If a local cause cannot be found for difficulty in the control of the bladder sphincter it is usually nervous in origin Direct questions should always be asked as to the presence of visual difficulties such as dimness of vision or diplopia Questions referable to the eighth nerve that is the presence or absence of tinnitus vertigo and deafness should be inquired about The history of the onset of an infection will often serve to make partially clear the type

## REFI RENCES

ALPERS B J Clinical Neurology Philadelphia F A Davis Co 1946

Association for Research in Nervous and Mental Diseases Schizophrenia (Dementia Præcox) New York Paul B Hoeber Inc 1928

BLEULER F Text book of Psychiatry translated by Brill The Macmillan Co 1924

BOND I D and SHURLEY J T Insulin Therapy and Its Future Am J Psychiat CIII 3 1946

FREEMAN W and WATTS J W Prefrontal Lobotomy Survey of 331 Cases Am Jour Med Sci CCXI 1 1946

HARROWES W McC The Depressive Reaction Types Jour Ment Sci 1933 79 17

HENDERSON D K and GILLESPIE R D Text book of Psychiatry Oxford Med Pub Oxford University Press 1927

HOCH AUGUST Benign Stupors New York The Macmillan Company 1921

JUNG C G The Psychology of Dementia Præcox Nervous and Mental Diseases Monograph Series No 3 1944

MEYER ADOLF The Nature and Conception of Dementia Præcox Jour Abnorm Psychol 1910 5 274

ROSE A S Review of Psychiatric Progress 1949 Am J Psychiat Jan 1950 106 592

ROSS T A The Common Neuroses New York Longmans Green & Co 1923

SARGENT W and SLATER E An Introduction to Somatic Methods of Treatment Baltimore Williams & Wilkins Co 1946

SONDEN TORSTEN A Study of Somatic Conditions in Manic depressive Psychosis Upsala 1927 Almquist & Wiksells Boktryckeri A B

STRECKER E A APPEL K E and APPEL J W Discovering Ourselves New York Macmillan Company 2nd ed 1943

STRECKER E A EBAUGH F G and EWALT J R Practical Clinical Psychiatry 6th Ed Philadelphia The Blakiston Co 1947

STRECKER E A and PEARSON M M Recognition and Management of the Beginnings of Mental Disease Oxford Medicine Oxford University Press 1948 7 948

than one seen in consultation in a hospital bed or at home In like manner the examination of patients on a ward service in hospitals will vary according to whether or not they are ambulatory The mental state of the patient can often be well evaluated during the interview His general emotional state the orderliness with which he gives his history, his memory and the presence or absence of such things as depression excitement and lethargy will be observed If he is delirious or comatose the history of the case will have to be given by someone else

After the mental status of the patient has been determined he should be weighed and his height taken He should then be completely undressed and the examination carried out in the following manner

SCHEME FOR NEUROLOGIC EXAMINATION

1 MENTAL STATUS Behavior disturbances of consciousness such as somnolence stupor or coma attention character and content of talk delusions illusions hallucinations emotional state orientation memory intelligence judgment insight Special tests such as the Binet-Simon

2 CRANIAL NERVES
 (a) *Olfactory* Sense of smell in each nostril
 (b) *Optic* Visual acuity—fundi examination Visual fields
 (c) (d) (e) (*Oculomotor trochlear abducens*) Equality of palpebral fissures movements of extraocular muscles nystagmus strabismus convergence
 Pupils—size shape equality regularity reaction to light direct and consensual reaction to accommodation
 (f) *Trigeminal* Sensory—sensation of the face corneal reflex Motor—action of the muscles of mastication
 (g) *Facial* Motor—voluntary and emotional movements of the facial musculature (peripheral and central types of facial palsy ) Sensory—taste over anterior two thirds of tongue
 (h) *Auditory* Acuity of hearing vertigo tinnitus Special tests such as Weber Bárány Rinné
 (i) (j) *Glossopharyngeal and Vagus* Sensory—taste over posterior third of tongue sensation of pharynx larynx gag reflex Motor—movements of palate swallowing phonation
 (k) *Spinal Accessory* Movements of sternocleido mastoid muscles and upper part of trapezius
 (l) *Hypoglossal* Movements of tongue

3 REFLEXES
 (a) *Superficial* Plantar cremasteric abdominal Tromner
 (b) *Deep* Patellar Achilles triceps biceps radial periosteal
 (c) *Visceral* Sphincter control sexual potency, priapism

4 MOTOR FUNCTIONS
 (a) Convulsions general or localized details about fits
 (b) Muscle power whether completely paralyzed or only weak Distribution of the involvement such as hemiplegia paraplegia and monoplegia Test strength of hands with dynamometer and other joints against resistance
 (c) Type of paralysis whether flaccid or spastic—muscle tone
 (d) Muscle atrophy or hypertrophy
 (e) Tremors or irregular movements such as fibrillary tremors athetosis chorea Parkinson s tremor, tics
 (f) Coordination tests finger to-nose test diadochokinesis heel to knee test
 (g) Station gait
 (h) Speech
 (i) Right or left handedness
 (j) Posture and attitude

5 TROPHIC FUNCTIONS
 (a) Muscular atrophy response of muscles to faradism and galvanism
 (b) State of skin eruptions ulcers glossy skin, herpetic eruptions bed sores arthropathies spontaneous or pathologic fractures

6 SENSORY FUNCTIONS
 (a) Subjective symptoms such as pain its type location radiation frequency conditions and postures relieving or aggravating it paresthesiae and dysesthesiae
 (b) Headache location type periodicity conditions aggravating it whether accompanied by nausea vomiting or vertigo
 (c) Tenderness hyperesthesia its location if present
 (d) Objective sensory tests for touch pain, hot and cold vibratory sense stereognosis sense of position deep pressure pain spot localization graphesthesia compass test All abnormal sensory results should be charted Objective sensory examination should be done when the patient and examiner are not tired or disturbed in a warm room preferably at the beginning of the examination and in the morning

7 VEGETATIVE NERVOUS SYSTEM
 (a) Cervical sympathetic size of the pupil enophthalmos exophthalmos narrowing of the palpebral fissure flushing or sweating of the face neck and upper extremities the reaction of the pupil to cocaine

of lesion from which the patient suffers Vascular accidents in the central nervous system usually produce sudden or apoplectiform onsets A tumor growing in the brain or the cord may take weeks or even years to produce the syndrome which the examiner sees, although it must not be overlooked *that occasionally the onset in a case of* spinal or brain tumor may apparently be sudden, the tumor may grow slowly and produce few or no symptoms until a hemorrhage suddenly occurs Because nerve fibers can function through a glioma, such a tumor may attain a large size before the symptoms are produced or before a hemorrhage suddenly occurs into it The progress of symptoms produced by an abscess is usually midway between a vascular accident and a tumor The relation, if any of a nervous condition to injury or an infection should be carefully inquired into Many patients with chronic encephalitis were but mildly ill with the acute attack which may have been entirely overlooked questions therefore, must be asked as to the occurrence of an illness characterized by double vision, *lethargy or perhaps insomnia* The sequence of events is an extremely important part of the history double vision occurring early in a history suggestive of brain tumor is of localizing importance, but if it occurs late *it may be simply a manifestation of a general* increase of pressure The character of a headache, if complained of should be closely scrutinized, and the index of suspicion of the examiner for such things as cerebral syphilis, brain tumor sinus disease and eye strain should be high If a spinal tumor is suspected the location of the original pain and the exact order of the development of symptoms is most necessary for a satisfactory diagnosis The examiner should be alive to the possibility that pain even though present in the abdomen or chest may be due to an involvement of a spinal root and that such a pain, because it is increased by coughing or sneezing, may simulate pleurisy *Root* pain is not as a rule, developed or aggravated by deep breathing

In obtaining the history of a patient suffering from convulsions it is important to inquire into aura, cry whether or *not he* injures himself in falling, bites the tongue, loses control of the urine and sleeps after an attack If there is a possibility that the *case may be hysterical the symptoms should* be put to the patient in a negative manner She should be asked "Of course, you never bite your tongue and never have a headache after a fit?" The same procedure should be *followed* when the abdomen or other parts are examined, not only by the student in neurology in search of knowledge, but also by the surgeon There can be no doubt but that many patients suffering from pain in the appendiceal region have it suggested to them by a surgeon who poking his finger into McBurney's point, asks in a suggestive tone, That hurts you doesn t it? The history of a paresthetic phenomenon is sometimes a great aid in arriving at a diagnosis Pernicious anemia and multiple neuritis are probably the commonest causes of numbness in the toes and fingers Questions should not be omitted pertaining to the general health of the patient Symptoms referable to the lungs heart and gastrointestinal tract should be particularly inquired into How the patient spends his *spare time if he has any* whether or not he has a hobby whether he plays golf and whether or not he takes too keen delight in the pleasure of the table may have a bearing on his condition and lead to a correct *evaluation of the symptoms* A good history is one of the most important things which leads to a correct diagnosis By the time a good history is obtained, certain leads will be indicated as to the location of the lesion and the type *of examination indicated* It is always wise however to have a definite examination routine which should not be neglected in the early years of practice For this reason some authorities believe that *only by taking a history and recording* the examination on a form will a complete and detailed result be obtained

When the *examination* is made it should be done in a routine systematic manner and *while there are many variations in* the method of starting an examination, much will depend upon the circumstances under which the patient is seen as to the exact order in which various tests should be done *It is obvious that a patient seen in an office* will be put through a little different routine

than one seen in consultation in a hospital bed or at home In like manner the examination of patients on a ward service in hospitals will vary according to whether or not they are ambulatory The mental state of the patient can often be well evaluated during the interview His general emotional state the orderliness with which he gives his history, his memory and the presence or absence of such things as depression excitement and lethargy will be observed If he is delirious or comatose the history of the case will have to be given by someone else

After the mental status of the patient has been determined he should be weighed and his height taken He should then be completely undressed and the examination carried out in the following manner

SCHEME FOR NEUROLOGIC EXAMINATION

1 MENTAL STATUS Behavior disturbances of consciousness such as somnolence stupor or coma attention character and content of talk delusions illusions hallucinations emotional state orientation memory intelligence judgment insight Special tests such as the Binet-Simon
2 CRANIAL NERVES
   (a) *Olfactory* Sense of smell in each nostril
   (b) *Optic* Visual acuity—fundi examination Visual fields
   (c) (d) (e) (*Oculomotor trochlear abducens*) Equality of palpebral fissures movements of extraocular muscles nystagmus strabismus, convergence
   Pupils—size shape equality regularity reaction to light direct and consensual reaction to accommodation
   (f) *Trigeminal* Sensory—sensation of the face corneal reflex Motor—action of the muscles of mastication
   (g) *Facial* Motor—voluntary and emotional movements of the facial musculature (peripheral and central types of facial palsy) Sensory—taste over anterior two thirds of tongue
   (h) *Auditory* Acuity of hearing vertigo tinnitus Special tests such as Weber Bárány Rinné
   (i) (j) *Glossopharyngeal and Vagus* Sensory—taste over posterior third of tongue sensation of pharynx larynx gag reflex Motor—movements of palate swallowing phonation
   (k) *Spinal Accessory* Movements of sterno cleido-mastoid muscles and upper part of trapezius
   (l) *Hypoglossal* Movements of tongue
3 REFLEXES
   (a) *Superficial* Plantar cremasteric abdominal Tromner
   (b) *Deep* Patellar Achilles triceps biceps radial periosteal
   (c) *Visceral* Sphincter control sexual potency priapism
4 MOTOR FUNCTIONS
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the nerve within the ball of the eye is the site of inflammation it is spoken of as *optic neuritis* There is no sharp line of demarcation between optic neuritis and choked disk or papilledema as far as the opthalmoscopic appearance is concerned however in optic neuritis the visual acuity is markedly impaired early and the fields show a central scotoma In papilledema visual acuity is usually only slightly diminished until late and the blind spot is enlarged The changes in the eye-ground which occur and which are of great importance from a neurologic point of view are atrophy optic neuritis and choked disk Optic atrophy is either primary or secondary Primary atrophy is due to direct involvement of the nerve It is usually bilateral and is a particularly common symptom in neurosyphilis especially tabes exogenous poisoning such as arsenic lead quinine tobacco carbon monoxide and above all alcohol These poisons act by producing a retrobulbar neuritis which leads in time to optic atrophy Infectious diseases may produce retrobulbar neuritis and the optic nerves may also be involved in multiple neuritis Retrobulbar neuritis is frequently the earliest manifestation of multiple sclerosis A large hemorrhage from any part of the body may occasionally produce optic atrophy

Inflammatory reactions or neoplastic conditions in or about the chiasm and suprasellar tumors often give rise to primary atrophy In fact the presence of optic neuritis or choked disk points decidedly away from lesions of the pituitary In amaurotic family idiocy (Tay-Sachs disease) optic atrophy occurs often with a characteristic cherry red spot in the macula area

A combination of optic atrophy on the side of the lesion and choked disk on the opposite side has been described in frontal lobe tumor

Retrobulbar neuritis is often followed by optic atrophy usually more marked on the temporal side of the disk Some time elapses before the pallor is seen The most characteristic visual field defect is bilateral central scotoma for red blue and green The visual affection is due to an interstitial neuritis of the papillomacular bundle Sphenoid and ethmoid diseases may produce either retrobulbar neuritis or optic neuritis Optic neuritis may occur also from any toxic or infectious cause such for example as kidney disease and diabetes The disk may be raised somewhat and the differential diagnosis between neuritis and papilledema may be a difficult one

Choked disk or papilledema is a not uncommon finding in cases with increased intracranial pressure The choking of the nerve occurs at the optic foramen Choking is characterized by overfilling of the veins contractions of the arteries swelling and blurring of the disk and by haziness of the margins A high degree of choking of the disks is compatible with good or normal vision but the visual acuity may be diminished In most cases of choked disks hemorrhages and exudates may be seen at the nerve head Choked disk is usually bilateral but may be more marked on one side At least 90 per cent of the patients suffering from choked disk have brain tumors Syphilis meningitis ependymitis sinus disease anemia infections and toxemias account for the remaining 10 per cent Enlargement of the blind spot and contraction of visual fields are common signs accompanying choked disk Each patient exhibiting choked disk should be considered as harboring a brain tumor until proved otherwise

The exact determination of the state of the visual fields is of the greatest importance in the localizing of cerebral lesions It is often advisable to repeat the examination particularly if the patient is dull or the examiner hurried A change may occur as a natural result of the disease which may clinch the localization

## Third Fourth and Sixth Nerves

The third nerve supplies all the muscles of the eyeball with the exception of the external rectus superior oblique and the dilator of the pupil The sphincter of the iris and ciliary muscles are supplied by the third nerve It also in part supplies the levator palpebræ The fourth (trochlear nerve) supplies the superior oblique whose function is to move the eyeball downward and outward The sixth nerve supplies the

(b) Neuralgia, angioneurotic edema, localized edema, cyanosis erythema, and temperature changes

8 SKELETAL SYSTEM Depressions, enlargements, tumors, investigation of the joints spinal column and mobility scoliosis, kyphosis tenderness

9 LABORATORY DATA

10 SPECIAL TESTS Electrical reactions of muscles Pneumo-encephalography Electro-encephalography Air or oil myelography Ventriculography Angiography Use of radioactive substances

## THE CRANIAL NERVES

### FIRST NERVE

Loss of smell (anosmia) may be due to disease in any part of the olfactory pathway

The sense of smell is tested by using volatile odoriferous substances such as oil of cloves coffee, camphor and peppermint Ammonia and acetic acid should not be used as they irritate the trigeminal nerve Each nostril is tested separately, the other being held closed

Since anosmia is commonly due to local nasal disorders such as polypi and acute rhinitis, little neurologic emphasis can be placed on a loss of smell unless local nasal pathology is definitely excluded In the absence of local disease unilateral anosmia may be of significance It occurs in fractures through the base of the skull in basal leutic meningitis in tumors which compress the olfactory pathways and in hysteria *Olfactory hallucinations usually of a disagreeable nature occur in the so called uncinate fits as well as in mental disease*

### SECOND NERVE

The examination of the optic nerve is one of the most important parts of the neurologic examination Vision may be tested by asking the patient to count fingers or by Snellen's test type Changes in the visual fields can be roughly determined by the examiner bringing into the field of vision from all directions his own hand the fingers of which are either moving or still In an aphasic or semi stuporous patient this can be done by the so-called feeding test that is, by bringing into the field of vision a spoon on which food has been placed If the patient sees it he will usually open his mouth More accurate determination of the visual field defect is obtained by perimetry or tangent screen studies The optic nerve can be seen directly with the ophthalmoscope, optic atrophy, either primary or secondary, may be detected as well as papill edema

Neurons of the optic nerves arise in the ganglion cells of the retina whence they pass in the optic nerve to the chiasm where the fibers from the temporal half of the retina continue on the same side whereas those from the nasal sides cross The optic tract fibers then terminate in the primary optic centers *i e*, external geniculate body, the pulvinar and the superior colliculus The last neuron in the course of the tract then goes to the occipital pole especially in the region of the calcarine fissure There is no further crossing of the visual pathways so that a lesion involving the optic tract anywhere behind the chiasm will produce contralateral homonymous hemianopsia, or a smaller defect if seen early The fibers for the reflex activity of the pupils run in the optic nerves and are both crossed and uncrossed A lesion anterior to the chiasm results in impairment of vision or in blindness on the same side A lesion at the chiasm such as, for example, that which is seen in pituitary tumors produces a bitemporal hemianopsia due to disturbance of the fibers supplying the nasal halves of the retina

*Binasal hemianopsia* is a rare finding It is due to bilateral lesions usually a syphilitic exudate at the lateral aspects of the chiasm or as a result of pressure from bilateral sclerotic calcification of the internal carotids Lesions in the optic tracts in or anterior to the primary optic centers may readily impair the pupillary reflex Lesions posterior to the primary optic centers do not do so being beyond the reflex arc Lesions deep in the temporal lobe or of the occipital lobes may give a contralateral quadrantanopsia

*The optic nerve may be implicated directly* by tumor syphilis fracture hemorrhage aneurysm or meningitis The nerve itself may be the site of a glioma Direct pressure on the nerve usually results in atrophy If the nerve is involved behind the eyeball the condition is called *retrobulbar neuritis* If

traction and dilatation of the pupil Loss of reaction of the pupil to light occurs in optic atrophy involvement of the third nerve and affections of the ciliary ganglion The loss of the direct reflex to light with preservation of the contraction of the pupils in accommodation for near objects is called the *Argyll Robertson phenomenon* and is a sign extremely suggestive of neurosyphilis It may however be seen in alcoholism arteriosclerosis multiple sclerosis and epidemic encephalitis but is extremely uncommon in those conditions An Argyll Robertson pupil is not necessarily completely paralyzed to light at the beginning but passes through different grades just as any other physical sign The reaction of the pupil to accommodation is the contraction of the pupil which is seen when the patient converges his eyes on a near object The loss of the contraction to accommodation with preservation of the light reflex is occasionally seen in epidemic encephalitis and after diphtheria The *paradoxical pupil* when the pupil dilates instead of contracting on exposure to light is infrequently seen in tabes The ciliospinal reflex which is the reaction of the pupil to painful stimulation of the skin of the neck thereby causing the pupil to dilate is of value in estimating the state of the cervical sympathetic Tonic pupils are found in Adie s syndrome Such pupils do not react to ordinary light but may constrict slightly with bright light The contraction and subsequent dilatation on removing the stimulus is very slow Their reaction to accommodation is markedly delayed Often only one pupil is affected Tonic pupils may be differentiated from the Argyll Robertson type by the fact that they respond normally to the instillation of eserine and homatropine

*Nystagmus* is an involuntary rhythmic tremor of the eyeballs usually bilateral and symmetrical It may be present when the eyeballs are looking straight ahead but is more likely to be developed when the patient looks upward downward or laterally It may be lateral vertical or rotary Nystagmus may be due to cerebellar disease defects in fixation due to extremely poor vision or stimulation of the labyrinths Nystagmus may occur from lesions of the mid brain pons and cerebellum and is frequently seen in such diseases as multiple sclerosis and Friedrich s ataxia Ocular nystagmus in which both phases or the movement are of equal rapidity is a fairly frequent finding in albinism and in patients with high myopia The so-called miner s nystagmus is seen in those who work for long periods in dim light Loss or disturbance of associated movements of the eyes upward or downward is an important localizing sign of disease of the anterior quadrigeminal bodies either directly or by pineal tumors Loss of lateral associated movements in which the eyes cannot be moved to one side is due to a lesion in or near the sixth nerve nucleus or the posterior longitudinal bundle on the side of the paralysis the failure of the opposite internal rectus to function properly is due to the loss of associated movements and not paralysis *Conjugate deviation* is due to loss of power of turning both eyes toward the sides opposite the lesion which is in or above the internal capsule The movements that are not paralyzed draw the eyes toward the side of the lesion

### Fifth Nerve

The trigeminal nerve is a mixed one The motor root supplies the muscles of mastication the tensor tympani tensor palati mylohyoid and anterior belly of the digastric The sensory fibers enter the pons and descend into the cervical cord to the second or third segment The Gasserian ganglion lies in the middle fossa on the petrous portion of the temporal bone The sensory root divides beyond the ganglion into three divisions The *first* or *ophthalmic division* conveys sensation from the eyeball and lachrymal gland the conjunctiva (except that of the lower lid) the skin of the forehead and scalp up to the vertex the mesial part of the skin of the nose and the mucous membrane of the upper part of the nasal cavity

The *second* or *superior maxillary division* conducts sensation from the skin to the upper lip the side of the nose and the adjacent parts of the cheek the lower eyelid and part of the temple It also innervates the conjunctiva of the lower lid the upper

external rectus muscle which moves the eyeball outward

Paralysis of any one of the ocular muscles will lead to double vision and a deviation of the eyeball The diplopia is due to the fact that the image, instead of falling on each retina at the same place, strikes at different points because of the inequality of the muscles Diplopia is present when both eyes are being used, although monocular diplopia, usually an hysterical phenomenon, may occur if a deformity of the cornea is present If the third nerve is completely paralyzed, the upper lid droops because of the paralysis of the levator palpebræ superioris Due to the unopposed action of the external rectus the eyeball is turned outward The eyeball cannot be moved upward, downward or inward, although a slight downward and outward movement can be performed by the superior oblique muscle which is supplied by the fourth nerve Since the third nerve supplies the sphincter of the iris the pupil is wide because of the unopposed action of the dilator which is supplied by the sympathetic The pupil does not respond to light, nor does the eye attempt *convergence* *The third nerve may* be completely paralyzed or partially affected Paralysis of the fourth nerve results in involvement of the superior oblique muscle, which turns the eyeball downward and outward and at the same time rotates the vertical meridian slightly inward at its lower end It is extremely difficult to detect a paralysis of the superior oblique nerve but it is usually determined by the diplopia which results when the patient attempts to look downward and outward The false image stands lower than the true and is especially likely to appear when the patient walks downstairs

The sixth nerve supplies the external rectus and involvement of it produces paralysis of that muscle The patient is unable to turn the eye outward beyond the midline All other movements are normal The diplopia is present when the eyes are directed toward the side of the paralyzed sixth nerve

## The Pupil

The things to be noted about the pupil are the size shape equality position and its reaction to light, to painful stimulation of the skin of the neck and to accommodation Slight inequality (*anisocoria*) may occur in individuals free of disease and, if it is the only abnormality present, may be disregarded If the inequality is considerable *and especially if accompanied by other* signs organic disease may be present The pupils are abnormally large in poisoning by certain drugs such as the atropine group alcohol and cocaine and in individuals who are under emotional stress *Mydriasis* may result from paralysis of the sphincter of the pupil or may be due to stimulation of the dilator The pupils in blind eyes are usually dilated A unilateral fixed dilated pupil may result from compression of the third nerve, by *herniation of the hippocampal* gyrus over the free edge of the tentorium in expanding intracranial lesions *Myosis*, or abnormal smallness of the pupil may occur from disease of the pons in tabes and in cervical cord lesions due to involvement of the cervical sympathetic The pupils may also be contracted as the result of iritis Pilocarpin and opium contract the pupil

The *shape of the pupil* should be carefully determined Unequal and irregular pupils, if *such local conditions as iritis operative* procedures and coloboma have been ruled out, are usually syphilitic in origin although postencephalitic states and cerebral arteriosclerosis are rarely causes of such changes The pupil may be ectopic Occasionally such a condition indicates a lesion of the mid brain Testing of the pupillary reflex to light is an important part of a physical examination Each eye should be tested separately because if the light is thrown in both eyes at the same time a pupil fixed to direct light might react consensually The light reflex depends upon the integrity of the reflex arc The fibers pass in the optic nerves to the *mid brain* and the efferent parts of the arc are made up of the third nerve and ciliary ganglion to the sphincter of the pupil

At times a phenomenon known as *hippus* is found This consists of a rhythmic con

seen in bulbar palsy where only the lower part of the face is involved even though the lesion is in the nucleus because as a usual thing, only the lower part of the nucleus is affected in such cases

### Eighth Nerve

The auditory nerve is composed of the cochlear and vestibular portions Paralysis of the cochlear portion of the nerve results in unilateral deafness The cortical representation of the eighth nerve is in the temporal lobe and the recognition and memory of words heard in the first temporal convolution on the left Involvement of the first temporal convolution will produce a condition known as *word deafness* in which while the patient is able to hear the sound the words are not recognized as such The auditory nerve is frequently pressed upon by tumors may be the seat of a toxic neuritis and may be involved in syphilis at the base, in meningitis or by any acute infections and it may be infiltrated in leukemia Hemorrhage or inflammatory reactions in the labyrinths may occur in any toxic or infectious state In a patient suffering from diminution or loss of hearing it is important to differentiate between nerve deafness and the deafness which arrives as a result of middle ear disease The differential diagnosis is made by a careful neurologic examination and the use of Weber s Rinne s and Schwabach's tests Tumors of the eighth nerve are common Involvement of the vestibular portion of the eighth nerve is exemplified by Meniere s disease or more properly *Meniere s syndrome*

Syphilis arteriosclerosis malaria and almost any infection or toxemia are capable of producing changes in the labyrinth Acute involvement of the labyrinth produces vertigo vomiting disturbance of the equilibrium and of the gait and pronounced nystagmus Any movement of the patient produces vertigo so intense that the patient may be thrown to the ground like a bolt Tinnitus and impaired hearing or even deafness are present and usually remain after the other symptoms have disappeared Diarrhea may also occur during an attack of acute labyrinthitis Tumors in the angle and syphilis of the base should always be excluded when Meniere s syndrome presents itself The acute attack may clear up, to be followed by signs of chronic labyrinthitis which is also often due to middle ear disease The symptoms may vary from tinnitus and slight deafness and vertigo to dizziness so intense that the patient is thrown to the ground The relief of these symptoms is very difficult Intracranial section of the vestibular branch of the eighth nerve has been recommended Meniere s syndrome is occasionally mistaken for epilepsy, but the dizziness deafness and tinnitus unaccompanied by unconsciousness which is rarely present should make the differentiation possible

### Ninth Nerve

Involvement of the glossopharyngeal nerve rarely occurs by itself If it should happen the symptoms would be loss of taste over the posterior third of the tongue dysphagia, loss of the pharyngeal reflexes and anesthesia in the upper portion of the pharynx

Glossopharyngeal neuralgia, a rather rare condition, is characterized by transient paroxysms of excruciating pain referred to the ear the tonsillar region pharynx or side of the neck These attacks are often brought on by swallowing or yawning A trigger zone probably exists in the Eustachian tube

### Tenth Nerve

Paralysis of the vagus nerve may be part of the symptom complex of bulbar palsy tumors of the bulb acute and chronic inflammations syringomyelia and multiple sclerosis The vagus nerve is occasionally acutely inflamed especially after attacks of diphtheria It is also involved though infrequently by poisons such as alcohol After the nerve emerges from the bulb it may be involved by neoplasms inflammatory reactions of the meninges vascular disease especially aneurysms and disease of the base of the skull It is occasionally injured during operations on the neck The recurrent laryngeal branch of the nerve may be cut during an operation on the thyroid and is frequently paralyzed by an aneurysm of the

teeth the mucous membrane of the upper lip, the upper part of the cheek, upper jaw, hard palate, uvula, tonsil naso-pharynx, middle ear and the lower part of the nasal cavity

The *third*, or *inferior maxillary division* contains, in addition to sensory fibers the motor root The sensory part of the nerve supplies the skin of the posterior part of the temple and the adjacent part of the pinna the anterior and the upper wall of the external auditory meatus, part of the cheek, the lower lip and chin the lower teeth and gums part of the tongue the floor of the mouth the inner surface of the cheek and the salivary glands

The taste fibers from the anterior two thirds of the tongue are contained in a branch of the third division They leave the lingual branch course along the chorda tympani and reach the facial nerve in the Fallopian aqueduct The taste fibers from the posterior third of the tongue are supplied by the glossopharyngeal nerve The tongue is tested in the anterior and posterior parts separately Substances such as quinine, vinegar, sugar and salt are used and are rubbed on the tongue With his tongue out the patient should be asked whether the substance is sweet salty bitter or sour and he should communicate his opinion to the examiner by a nod of the head Loss of taste is called *ageusia* The important reflexes in the domain of the fifth nerve are the corneal sneeze and conjunctival The *corneal reflex* is elicited by touching the cornea with a probe padded with cotton or with the head of a pin Care should be taken not to touch an eyelash or to bring the testing object over the pupil, because in either event the patient will blink Both corneal reflexes are lost in anesthesia and coma The sensory part of the arc is the fifth nerve and the motor part is the seventh If the corneal reflex is lost from a lesion of the fifth nerve neither eye will blink If the reflex is lost from a lesion of the seventh nerve the pain produced by the corneal contact will cause the other eye to blink Loss of the corneal reflex is the earliest sign of involvement of the sensory part of the fifth nerve The *conjunctival reflex* is taken in much the same way except the conjunctiva is touched rather than the cornea The *sneeze reflex* is tested by irritating the nasal mucous membrane with a probe padded with cotton The normal individual or the hysteric whose fifth nerve is intact, will sneeze If the motor root is paralyzed the temporal fossa is hollowed and the masseter wastes When the patient is instructed to close his mouth the affected muscles do not harden under the examiner s fingers When the patient opens the mouth the jaw is pushed toward the paralyzed side This occurs because the external pterygoid fails to draw the condyle forward on the affected side Trophic disorders may occur on the side of a fifth nerve paralysis the secretion of tears of saliva and of nasal mucus is diminished and thereby the functions of those parts are interfered with The teeth may become loose on the side of the trophic lesion and fall out Neuroparalytic keratitis may occur on the affected side Facial hemiatrophy and hypertrophy are thought by some to be due to trophic lesions of the fifth nerve but removal of the Gasserian ganglion has not been known to produce hypertrophy or atrophy of the face

## Seventh Nerve

The facial nerve supplies all the muscles of the face with the exception of the levator palpebræ superior, down to and including the platysma The nerve contains the taste fibers of the chorda tympani and deep pressure pain fibers for the face The nerve is frequently paralyzed by infections exposure to cold, tumors of the parotid middle ear disease tumors of the cerebellopontile angle and syphilis in the angle Two types of *facial paralysis* are to be distinguished In peripheral facial palsy due to involvement of the peripheral nerve or nucleus the entire side of the face is involved The patient is unable to close his eyes wrinkle his forehead smile whistle or puff his cheeks In a central facial palsy due to a lesion of the pyramidal tract the upper part of the face is unaffected but in showing the teeth or smiling a weakness is noted on the affected side Sometimes a normal facial asymmetry may be mistaken for a slight central facial palsy An exception to the above rule is

tained On the other hand if the stimulation is too great a mass of reflexes will occur from which nothing can be learned It is frequently necessary to attract the patient's attention while this reflex is being taken Occasionally the reflex may be obtained when the skin of the heel is irritated or by drawing a pin across the ball of the foot In the person with an intact pyramidal system the great toe flexes If the pyramidal tract or the leg center in the cortex is affected by disease or injury the great toe extends The more slowly and more isolated the extension is the more typical is the reflex There may be other movements of the toes such as flexion extension or fanning but it is the movement of the great toe which distinguishes the reflex The extensor plantar reflex (Babinski's sign) is always pathologic except in infants whose pyramidal tracts are not yet myelinated and means interruption in some degree at least of the functions of the pyramidal tract The abnormal plantar reflex may occur after an epileptic fit and in uremia diabetes or alcoholism There are many modifications of the Babinski reflex such as the Oppenheim Chaddock and Gordon reflexes all of which mean the same The Babinski *reflex has done a great deal to differentiate* between organic and hysterical conditions If the plantar reflex arc is interrupted for example by loss of sensation or by a peripheral paralysis of the flexors of the toes no plantar response will be obtained

In the upper extremity a reflex somewhat comparable in its significance to the Babinski reflex has been described by Tromner and by Hoffman With *the patient's forearm* and hand midway between pronation and supination the left hand of the examiner supports the forearm and the nail of the middle finger is slightly stroked and flicked toward the palm If the pyramidal tract is normal the thumb or index finger does not move but if the pyramidal fibers are involved the thumb and index finger approach each other and the distal phalanx of the index finger or thumb or both move in flexion This reflex does not have the specific pathognomonic significance of Babinski's sign the sign may appear and disappear in some patients who have been observed for years without showing any other evidence of organic neurologic disease It is not infrequently *found* in neurotics especially in those with marked anxiety and muscular tenseness along with hyperreflexia

The *abdominal reflexes* appear after the pyramidal tracts are myelinated They are normally present except in the obese and in those whose abdominal walls are relaxed and atonic for any reason the most important of which is pregnancy The loss of the reflex is common in acute abdominal conditions It is obtained by stroking the skin of the abdomen parallel with Poupart's ligament and the costal border Any blunt object may be used but a pin produces best results The reflexes are called the upper and lower and the segments of the cord concerned are the eighth to the twelfth dorsal The reflex consists of a dimpling or a pulling of the skin and movement of the umbilicus toward the stroked side due to contraction of the abdominal recti muscles In a healthy individual with normal abdominal walls loss of reflex means an interruption in the reflex arc such as might occur for instance in anterior horn disease It may also be due to involvement of the pyramidal tract and is therefore a frequent sign of hemiplegia In the presence of other signs the absence of abdominal reflexes in a young individual is suggestive of multiple sclerosis The abdominal reflexes are lost on the paralyzed side if the pyramidal tract lesion is above the eighth dorsal segment

The *cremasteric reflex* is obtained by stimulating the skin of the upper and inner *side of the thigh which produces an elevation* of the testicle on that side Its loss has the same significance as the abdominal reflex The segments in the cord concerned with this reflex are the first and second lumbar

The important *deep reflexes* (sometimes called tendon) are the patellar Achilles triceps and biceps Complete relaxation of the muscles concerned in a reflex must be obtained and the reflexes that are not obtainable while the patient is in bed should if possible be tested when the patient is up before they are considered lost Involvement of either the sensory or motor component of the arc will cause a diminution or

aorta, by dilatation of the left auricle such as occurs in mitral stenosis and by neoplastic masses in the mediastinum Paralysis of the tenth nerve produces unilateral paralysis of the palate, pharynx and larynx which produces a nasal quality of the voice and slight dysphagia The soft palate is immobile and is lower than normal and the palatal and pharyngeal reflexes are absent The homolateral vocal cord is in the so-called cadaveric position, and fails to move during phonation and respiration The cardiac rate and rhythm are not altered and abdominal symptoms are usually absent Bilateral recurrent paralysis is usually central in origin and causes complete loss of voice, respiration is difficult stridor and dyspnea are usually pronounced and there is lack of closure of the glottis in coughing Involvement of the tenth nerve is often associated with implication of the ninth eleventh and twelfth

### Eleventh Nerve

The spinal accessory nerve is a motor one consisting of two parts, the medullary and spinal The bulbar part of the nerve is really part of the vagus The eleventh nerve supplies the sternomastoid and the trapezius In general, it is affected by the same things which cause involvement of the ninth and tenth nerves and also by affections of the upper cervical cord It is not infrequently cut during operations on the neck The paralysis of the nerve produces inability to turn the head toward the opposite side and the head deviates to the affected side when the chin is forced downward against resistance Involvement of the trapezius produces a drooping of the shoulder on the paralyzed side, alteration of the outline of the neck, shrugging of the shoulder is interfered with, and the scapula cannot be brought to the midline The scapula is displaced down and out The affected muscles are atrophic and show alterations to the electrical reactions

### Twelfth Nerve

The hypoglossal nerve is a motor nerve supplying the muscles of the tongue The tongue is usually involved in ordinary cases of hemiplegia, in which it deviates to the side of the paralysis, on protrusion It does this because of the action of the uninvolved glossal muscle which pushes the tongue out and toward the opposite side It is practically always involved in bulbar palsy and is vascular and inflammatory reactions in the bulb Tumors of the bulb and the diseases of the spinal cord especially amyotrophic lateral sclerosis and syringomyelia, may be complicated by involvement of the twelfth nucleus Syphilis of the bulb or at the base of the brain may implicate the twelfth nerve Nuclear disease such as is produced by bulbar palsy, is practically always bilateral Outside of the skull the nerve may be involved by malignant disease trauma, disease or injury to the atlas and aneurysm of the carotid artery The affection of the nerve produces a paralysis of the tongue on the side of the lesion The tongue appears wrinkled and atrophic the electrical reactions are reversed and fibrillary tremors are usually pronounced although they may be absent in peripheral involvement If only one twelfth nerve is paralyzed the ability to eat is not affected but, if the tongue is paralyzed on both sides eating is difficult and speech which is also little affected by unilateral paralysis is seriously involved

## THE REFLEXES

The examination of the reflexes is a necessary part of each neurologic survey of an individual One of the most important is the *plantar reflex* which with the abdominal and cremasteric make up the important superficial reflexes To obtain the plantar reflex the patient should be recumbent the foot should be warm externally rotated and grasped firmly at the ankle by one of the examiner s hands The sole of the foot should then be stimulated at the junction of the outer and middle thirds beginning at the heel and going forward Practically any small object may be used, but the best is a pin The least amount of stimulation necessary to bring about a response should be employed If too light stimulation is used no reaction whatsoever will be ob

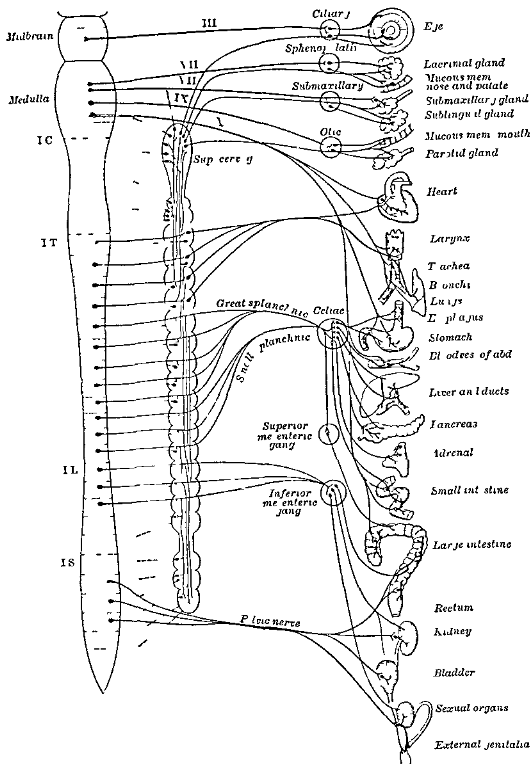



Diagram of efferent autonomic nervous system Blue cranial and sacral outflow parasympathetic Red thoracolumbar outflow sympathetic ----- Postganglionic fibers to spinal and cranial nerves to supply vasomotors to head trunk and limbs motor fibers to smooth muscles of skin and fibers to sweat glands (Modified after Meyer and Gottlieb) This is only a diagram and does not accurately portray all of the details of distribution *

* Manifestations due to disturbance in the autonomic system are discussed in the pertinent sections For a brief presentation of the manifestations due to involvement of the sympathetic and parasympathetic system the reader is referred to Frank L Apperly Patterns of Disease on the Basis of Physiologic Pathology J B Lippincott Co 1951 p 395 Editor

disappearance of the reflex. Thus, lesions of the peripheral nerves, of the spinal roots, of the posterior and anterior horns will cause a *diminution or loss of the deep reflex* at the level of the lesion. Involvement of the anterior horn cells of the cervical cord will not, of course, affect the reflexes of the lower extremities. A reflex may also be lost because of disease of the muscles, as in muscular dystrophy, where the reflex disappears as the muscle atrophies. The deep reflexes are exaggerated in disease of the pyramidal tracts, in functional nervous disorders, especially hysteria, and in cases where anxiety is a prominent symptom, in disease of the joints, after exercise, and in stimulation of the nervous system from the excessive use of tea, coffee and alcohol. It is only in disease of the pyramidal tract, however, that the Babinski sign occurs. A generalized increase in the deep reflexes without Babinski's sign or ankle clonus is not of nearly as much importance as the diminution, loss or inequality of the reflexes.

The *biceps reflex* is obtained by tapping the biceps tendon. The *triceps reflex* is obtained by striking the triceps tendon.

The best position in which to obtain the *patellar reflex* is to have the patient sitting in a chair with the feet flat on the floor. The patellar tendon should then be located, one of the examiner's hands placed on the thigh while the other wields the hammer which should strike the tendon a sharp, quick blow. If the reflex is difficult to obtain or is diminished, it may be brought out by reinforcement. In the case of the patellar reflex this may be done by having the patient squeeze his hands at the count of three, or better yet, by having him press downward with the ball of his foot as the patellar tendon is tapped. The *Achilles reflex* is obtained by having the patient kneel on a chair with the feet hanging over the seat, or by having him rest his hands on a desk or chair while flexing one leg off the floor. The examiner supports the foot at the ankle and taps the tendon of Achilles. A jar may be misinterpreted as a reflex.

The segments with which the important deep reflexes are concerned are as follows:

Biceps, fifth and sixth cervical.
Triceps, sixth and seventh cervical.
Patellar, second to fourth lumbar.
Achilles, fifth lumbar, first and second sacral segment.

*Ankle clonus*, which is frequently seen in pyramidal tract disease, and which consists of a rhythmic contraction of the soleus muscle, is obtained by having the knee moderately flexed. The examiner then sharply extends the foot, exerting pressure on its ball. A pseudoclonus may occasionally be found in hysteria.

The *vegetative* or *visceral reflexes* (vesical, rectal and genital) are due in most part to contraction of involuntary muscles; their centers are in the sacral cord, below the third sacral segment, and in the sympathetic nervous system. The *cilio spinal reflex*, which is brought out by pinching the skin of the neck, consists in a dilation of the pupil *on the ipsolateral side, and is due to stimulation of the cervical sympathetic*. Pressure backward on the eyeballs produces the *oculo-cardiac reflex* by which the rate of the pulse is slowed. (Plate 10.)

## THE MOTOR SYSTEM

Involvement of the motor system produces loss of or impaired power. The patient will often indicate where the weakness or paralysis exists. All of the muscles should be tested against resistance and the power of the hands should be determined with a dynamometer. An apparent loss of power may occur in hysteria, and power may be weak in the presence of muscles apparently splendidly developed, such as occurs, for example, in pseudohypertrophic muscular dystrophy. To examine properly the muscular system the individual muscles should be observed and palpated. It should be noted whether or not the muscles are normal, flabby or atrophic.

Atrophy of the muscles may be due to lesions of the peripheral motor nerve, anterior root, anterior horn cells, disease of the muscles themselves (such as dystrophy), bone and joint disease and wounds of an extremity, which produce the so-called muscular reflex atrophy. Atrophy of muscles rarely occurs from a cerebral lesion except in lesions of the parietal lobe; the *atrophy* is on the contralateral side of the lesion, is not severe and must be differentiated from wasting produced by disuse and ankylosis.

of joints Lesions of the motor peripheral nerve produce a flaccid atrophic paralysis with loss of reaction to faradism and equalization or reversal of the polar reactions in galvanism The deep reflexes in the distribution of the paralysis are lost or decreased Fibrillary tremors occur in the atrophic muscles if the lesion is in the anterior horn cells occasionally does an involvement of the peripheral nerve produce this phenomenon Fibrillary movements of the muscles are of great significance if they occur with other signs of organic disease It is a common symptom in the tongue in bulbar palsy and in muscles wasting from anterior horn disease Fibrillary tremors or muscle quivering are also seen in neurasthenic, poorly nourished individuals and in those who take tea, coffee alcohol or tobacco to excess In such instances the tremors are especially common in the deltoid biceps the large muscles of the thighs and of the eyelids Anterior horn symptoms always occur at the level of a lesion The atrophy which occurs in bone or joint disease is usually limited to a segment of the extremity involved but it may implicate the entire extremity The neighborhood deep reflex may be increased but Babinski s sign fibrillary tremors and reactions of degeneration do not occur If the joint disease is bilateral and produces reflex atrophy the case may be mistaken for amyotrophic lateral sclerosis A lesion of the anterior root will simulate closely that due to involvement of the anterior horn with one important exception fibrillary tremors are not present

*Paralysis* means a loss of power due either to functional or structural interruption in any part of the motor path and including the muscle itself *Paresis* means a weakness The two are often used rather loosely The term paralysis is often incorrectly employed when partial loss of power is meant

Paralysis of a mixed nerve will produce both motor and sensory loss To recapitulate a lower motor neuron disease produces flaccid paralysis of muscles supplied by the nerve anterior root or anterior horn cells and later atrophy develops The local deep reflex is lost and the response to faradism is absent Galvanism response is slow and with a reversal of the polar reactions Fibrillary tremors occur in anterior horn disease but not as a rule, in disease of the peripheral nerves

The *tone of an extremity* weakened or paralyzed by involvement of the voluntary motor pathway anywhere in its course from the motor cortex to the lower part of the cord is usually increased The paralysis or weakness which occurs is below the level of the lesion if this is above the decussation in the bulb, the paresis is on the contralateral side Below the pyramidal decussation the weakness which ensues is on the side of and below the lesion If both pyramidal tracts are involved above the decussation the condition is referred to as *diplegia* A lesion in an internal capsule produces weakness or paralysis of the opposite side, face arm and leg (*hemiplegia*) A complete lesion of the spinal cord in the cervical cord will produce *tetraplegia* or as it is called by some *quadriplegia* Implication of both pyramidal tracts of the spinal cord below the second dorsal will produce a *crural paraplegia* Paralysis of both upper extremities from a cord lesion is referred to as a *brachial paraplegia* and though rare may occur for example from acute anterior poliomyelitis or from occlusion of the anterior spinal artery

Paralysis of one extremity called *monoplegia* is the result of a cerebral spinal or peripheral lesion or of hysteria If part of an extremity is paralyzed as the result of a cerebral lesion the condition has been called by Spiller *segmental monoplegia* In pyramidal tract disease, particularly in cortical involvement movements and not muscles are paralyzed The deep reflexes are increased and various types of clonus may be elicited such as ankle patellar or wrist clonus The plantar reflex is of the extensor or Babinski type The muscles do not become atrophic from upper motor neuron palsy, but atrophy may develop if ankylosis of a joint or arthritis occurs on the paralytic side The muscles react normally to electricity In progressive pyramidal tract involvement with total paralysis especially in cases in which the cord has been injured or is pressed upon from without for example by Pott s disease

tempting the finger to nose test the patient overshoots the mark producing a symptom called *hypermetria* If a vertical line is drawn on a sheet of paper and the patient tries to draw a series of horizontal lines to the vertical line he overshoots or under shoots the mark The *rebound phenomenon of Holmes* is elicited in the following manner if an attempt is made by the examiner to extend the forearm against resistance and the force is suddenly discontinued the hand rebounds unchecked against the shoulder Another characteristic symptom of cerebellar disease is *adiadokokinesis*, which means a loss of the ability rapidly to perform a movement which calls into play antagonistic groups of muscles This symptom is elicited by having the patient rapidly pronate and supinate his hands or slap his palms and the extensor surfaces of the hands alternately against his knees In cerebellar disease, the patient performs these movements in an incoordinate fashion Cerebellar catalepsy is a very rare symptom It should be emphasized that there is no loss of sensation and no loss of power in the sense that it occurs in upper or lower motor neuron disease

*Cerebellar fits*, originally described by Hughlings Jackson are tonic in type and in reality the picture of decerebrate rigidity is produced Cerebellar fits due to involvement of the vermis, are bilateral those due to involvement of one of the cerebellar lobes are unilateral and on the side of the lesion

## Gait

Although all disturbances of gait are not exclusively due to involvement of the motor system they will be discussed under that heading

In testing a patient s gait he should be told to walk across the room preferably in a straight line and to turn sharply and walk back In spastic crural paraplegia the lower extremities are moved stiffly the steps are short the toes are scraped along If there is pronounced adductor spasm the so called scissor gait occurs in which the feet are alternately placed one in front of the other This gait may also be seen in bilateral cerebral lesions In a spastic gait occurring in paraplegia the soles of the shoes at the toe are worn off long before the rest of the shoes and the uppers are scuffed at the toes due to catching those parts in going upstairs In the hemiplegic gait the lower extremity on the affected side is swung from the hip the joints are flexed little or not at all and the anterior part of the foot is scraped on the ground In addition the upper extremity is held in a characteristic attitude The steppage or high stepping gait is that which occurs in a patient suffering from foot-drop, due especially to lesions of the anterior horns or the peripheral nerves and occurring in its best illustration in multiple neuritis and poliomyelitis A lesion of one popliteal nerve may produce a unilateral steppage gait In the steppage gait, the extensors of the toes and feet being paralyzed the patient must raise the knees high to make the toes and feet clear the ground and, as the feet come down they make a flip-flop sound due to the striking of the anterior part of the foot first and the heel second The gait of muscular dystrophy produces the duck or waddling gait quite similar to that seen in double congenital dislocation of the hips In this gait the feet are more widely separated than normally and a distinct lordosis occurs The ataxic gait is seen in tabes dorsalis in some patients with multiple neuritis and in any condition which involves the posterior columns such as the combined sclerosis of pernicious anemia The patient s walking base is widened, he lifts the feet jerkingly and suddenly throws them too wide and too high and then stamps the heels to the ground An ataxic gait can be told not only by sight but also by hearing since he makes a very characteristic stamping noise as he walks To re-enforce his faulty position sense his eyes are glued to the ground he has difficulty in walking a straight line and in proceeding with the eyes shut in the dark or backwards When the pyramidal tracts and posterior columns are both involved in the same patient for example in the combined sclerosis of pernicious anemia the gait assumes an element of both spasticity and ataxia A reeling or drunken gait is significant of cerebellar disease and if the cerebellar involvement is unilateral the patient has a

or a tumor, the reflexes of defense or spinal automatism may occur Thus, in a totally paralyzed extremity, even in one in which sensation may be completely abolished, sharply flexing the toe (*Strümpell's phenomenon*) or irritating the extremity up to a level corresponding to the height of the lesion will cause the paralyzed extremity to be sharply withdrawn That is, the foot and toe are extended and the knee and hip flexed This may be mistaken for a voluntary movement, especially if the idea is entertained that the patient is hysterical It is a bad prognostic omen, unless the cause can be removed, and is not a sign of returning power

If the pyramidal tract fibers to an extremity *are completely obliterated*, by a complete transection of the spinal cord, there is a flaccid paralysis of the extremity below the lesion with a loss of the deep reflexes and a plantar reflex of the flexor type or the plantar reflex may be absent, the so-called *Bastian's law* This is seen in its most typical form in paralysis coming on suddenly as the result of injury It may, however, be due to disease

Paralysis may be crossed, that is part of *the paralysis is on one side of the body* and part on the other due to a single lesion for example, a lesion in the right cerebral peduncle will produce a third nerve palsy on the side of the lesion and implication of the face, arm and leg on the opposite side (*Weber's syndrome*) *If in addition, there is* a tremor of the weak or paralyzed side of the body, it is referred to as *Benedikt's syndrome* The third nerve fibers the pyramidal tract and the red nucleus are implicated A lesion in the pons at the level of the facial nucleus will bring about facial paralysis of the peripheral type on the side of the lesion and of the arm and leg on the contralateral side Usually the ipsilateral *sixth nerve* is also involved giving rise to an internal strabismus on the side of the lesion (*Millard-Gubler syndrome*) A crossed sensory paralysis may occur in occlusion of the posterior inferior cerebellar artery with a loss of pain, heat and cold on the side of the face corresponding to the lesion and on the opposite side of the body

The increased tone in pyramidal tract disease is supposed to be due to release of the cortical inhibition Increased tone, even rigidity, may be seen in lesions of the extra pyramidal system The most intense rigidity which one of the writers has ever seen was in a case of bilateral lenticular degeneration *due to carbon monoxide poisoning* all of the joints including the jaws were so stiff that it was impossible *to move* them Despite the intense rigidity in such cases Babinski's sign is not present If the increased tone, however, is accompanied by an irregular movement such as chorea or athetosis, extension of the great toe may occur coincidentally as the foot is stimulated The extra pyramidal system when involved, produces in addition to *rigidity some type of irregular movements* as choreiform movements and athetosis In paralysis agitans the rigidity is of the cog wheel variety, and automatic movements such as blinking and the swinging of the arms in walking are lost or impaired

A combination of upper and lower motor neuron disease may occur in the same individual thus disease or injury to the cervical cord may produce paralysis of the anterior horn cells with resulting signs at the level *of the lesion Implication of the pyramidal* tracts at the same time will produce a spastic paralysis below this is not an uncommon finding in syringomyelia Involvement of the lumbosacral cord will cause a *flaccid* atrophic paralysis at the level of the lesion *Disease of the muscles themselves* such as occurs in progressive muscular dystrophy produces weakness and ultimately paralysis of the affected parts The nervous system is intact in this disease There are no sensory losses and the reflexes and electrical reactions disappear with the muscles Certain muscles especially the deltoids and those of the calves may be the site of pseudo *hypertrophy*

Involvement of the cerebellum or its tracts does not produce disturbance of sensation but causes *incoordination* The *function of the cerebellum is to coordinate* and to make even and smooth voluntary motor impulses This makes for *synergic movements* If this element is lacking the movement becomes jerky, ataxic and asynergic The movements are not synchronized and occur separately and disjointedly At

tempting the finger to nose test the patient overshoots the mark, producing a symptom called *hypermetria* If a vertical line is drawn on a sheet of paper and the patient tries to draw a series of horizontal lines to the vertical line he overshoots or undershoots the mark The *rebound phenomenon of Holmes* is elicited in the following manner if an attempt is made by the examiner to extend the forearm against resistance and the force is suddenly discontinued the hand rebounds unchecked against the shoulder Another characteristic symptom of cerebellar disease is *adiadokokinesis* which means a loss of the ability rapidly to perform a movement which calls into play antagonistic groups of muscles This symptom is elicited by having the patient rapidly pronate and supinate his hands or slap his palms and the extensor surfaces of the hands alternately against his knees In cerebellar disease the patient performs these movements in an incoordinate fashion Cerebellar catalepsy is a very rare symptom It should be emphasized that there is no loss of sensation and no loss of power in the sense that it occurs in upper or lower motor neuron disease

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tendency to veer toward the side of the lesion

The variety of gait frequently seen in elderly people with multiple areas of cerebral softening is the gait of "little steps" in which the patient takes short quick steps, often with evidence of spasticity on one or both sides Patients suffering from marked chorea, either Sydenham's or Huntington's but especially the latter, have a peculiar bizarre gait, which is caused by the irregularly appearing choreiform movements in the muscles of the lower extremities the pelvic girdle and the trunk This causes the patient to sway or pitch now to one side, now to the other, or perhaps forward The gait and also the posture of Parkinson s disease is characteristic The upper extremities are flexed at the elbows wrists, arms and hands which are held in the writing position The trunk and neck are flexed Often as he arises from a chair and before he is started in walking he takes involuntary steps laterally or backward When he is fairly well advanced in the disease he then shows the shuffling festinating gait which is so significant of the illness As he walks, the gait becomes faster and faster the patient appears to be pushed forward until finally he has to grasp hold of something so that he may stop and rest No matter how marked the festination it is unusual for a person with paralysis agitans to fall

In testing the gait much can be learned, not only from the manner in which the patient walks but also from the ease and facility with which he turns because in turning the first disturbance in gait may be seen The gaits of hysteria are many and varied *Astasia abasia* is used to describe that symptom of hysteria in which a patient capable of moving the lower extremities can neither stand nor walk In hysterical hemiplegia the affected foot is pushed or dragged along and rigidity of the joints or scraping of the foot along the floor is not found as it is in organic hemiplegia Hysterical disturbances of gait may be grafted upon an organic disease A person with hysterical disturbance of gait can often, by suggestion be made to walk much better backward than forward, whereas all organic gaits are made worse by walking backward

Involvement of the middle lobe or vermis of the cerebellum produces in the gait a tendency to fall forward or backward and often the asynergia of the trunk muscles is so great that it is impossible for the patient to walk at all

Involuntary and irregular movements are usually indicative of basal ganglia disorders and are seen in paralysis agitans progressive lenticular degeneration athetosis chorea, spasmodic torticollis

*Myoclonus* is a shock like contraction of the muscles occurring at regular or irregular intervals and varying from two or three a minute to one almost every second This is a common symptom in epidemic encephalitis The abdominal muscles especially are involved *Hiccough* is a myoclonic contraction of the diaphragm due to excitation of the inspiratory center Hiccoughing is a common symptom in encephalitis, but may be a result of other toxemias or occur reflexly from visceral disturbances

## Tremor

Tremor may be defined as an involuntary rhythmic movement of a part of the body, resulting from the contraction of muscle groups Tremors may be simple, in which only a single muscle group is involved, or may be compound where several muscle groups are affected They may be rapid or slow and may be increased or diminished by action Like all other involuntary movements they stop during sleep Tremors may be seen in exophthalmic goiter alcoholism and with excessive use of tobacco tea and coffee Emotional excitement especially fear may produce a generalized simple tremor Senile tremor may resemble closely that of Parkinson's disease but usually occurs bilaterally from the onset the rigidity of Parkinson s disease is absent This tremor is usually not affected or increased by action A senile tremor also affects the head and face more than the usual paralysis agitans tremor In some individuals a tremor of the head speech and upper extremities seems to be hereditary Tremors of the head accompanied by nystagmus may occur in poorly nourished rachitic children (spasmus nutans)

## SENSATION

Much may be learned about the sensory condition of a patient with no other instrument than a pin and even test tubes of hot and cold water may be needless luxuries Testing of sensation is the most trying part of a neurologic examination and it is imperative that both the examiner and the patient be free of fatigue and irritation The best time to do a sensory examination is early in the morning Outside distractions should be prevented the room in which the examination is made should be warm interruptions should not be allowed and the patient himself should be warm relaxed and in the recumbent position To diagnose and to localize lesions which cause sensory changes it is necessary to understand the pathways by which the sensory tracts ascend Most of the peripheral nerves are mixed and involvement of them produces in addition to paralysis loss of sensation which will of course correspond to the distribution of the particular nerve involved If all of the nerves of an extremity are involved the sensory loss is always most marked in the distal segment of the extremity and all forms of sensation are involved It is rarely that a dissociation sensory loss occurs from a lesion of a peripheral nerve but such a thing occasionally occurs in postdiphtheritic multiple neuritis In this condition however there is a possibility that the posterior columns of the cord may be affected The sensory fibers pass into the posterior roots and thence to the cord Involvement of a posterior root produces irritative sensory phenomena in the distribution of that particular root This is the nature of a pain usually of the sharp cutting type so common in tabes dorsalis The *pain is increased by sneezing coughing* or jarring and if it occurs in the chest it is often mistaken for pleurisy or angina If it is in the abdomen it is frequently thought to be appendicitis or some other acute abdominal condition and if it occurs in an extremity it is called neuritis rheumatism or sciatica As the root becomes more involved a loss of sensation occurs The form of sensation lost earliest and most frequently is *pain* so that in time the patient has an area in which he has a great deal of pain but in which pain sense itself is diminished delayed or lost The painful areas referred to the skin due to posterior root involvement may be small and of the so-called spot variety which are common in tabes dorsalis When the root enters the spinal cord the fibers relaying sensation from the muscles tendons joints and bones all the so-called gnostic sensations enter the posterior columns and ascend uncrossed to the gracilis and cuneate nuclei on the ipsolateral side of the medulla Shortly afterward the fibers cross the midline in the internal arcuate fibers thus forming the sensory decussation of the fillet They then pass through the crus to the optic thalamus where the fibers are again separated most of them end in the thalamus and some continue to the postrolandic area

*Deep pressure pain* is obtained by pressing on an area until the patient complains of pain or discomfort *Touch* in ordinary practice can be tested with the examiner's finger which should be stroked as lightly as possible on the area to be tested a wisp of cotton a camel hair brush or a feather may also be used *Heat* and *cold* are usually tested by test tubes filled with hot or cold water and the tubes applied in an irregular manner to the skin In all sensory examinations the patient should be blindfolded or should not be permited to see what is going on The sense of position or joint or posture sense is tested by moving passively a joint into various positions The part being moved should be grasped laterally For example if the sense of position being tested in the toe it should not be pushed upward or downward but should be grasped on either side and pulled in the desired direction This is important because a patient may have disturbance in the sense of position but if other forms of sensibility are normal he will be able to appreciate that his toe is pushed upward or downward When the member being tested is placed in a position the patient is then asked to describe the position in which it has been placed

Vibratory sense is tested by means of a tuning fork 128 C which having been set into vibration is placed upon a bone The normal patient says he feels a thrill

whereas the one with loss of vibratory sense feels nothing *Stereognosis* is the ability of an individual to recognize an object placed in the hand, by appreciation of its weight, size shape or texture Loss of stereognostic perception may occasionally be due to a peripheral nerve lesion, but is more often the result of involvement of the parietal cortex, the optic thalamus or the posterior columns of the cord Lesions of the posterior columns which produce complete loss of position and vibratory sensation do not cause much, if any loss of touch This is a common finding, for example in the combined sclerosis of pernicious anemia The ability of a person to determine the exact location of a spot which is touched goes closely with the position sense and is lost in a lesion of the parietal cortex

The fibers for temperature and pain cross through the central part of the cord almost immediately and ascend on the opposite side in the spinothalamic tract They ultimately reach the thalamus and are redistributed for discrimination to the cortex Cortical lesions will rarely produce much disturbance of pain heat and cold sensations whereas a lesion of the thalamus does cause a severe diminution or loss of these forms of sensation Most of the fibers for light touch and deep pressure cross the cord immediately and ascend to the thalamus anterior to the spinothalamic tract The loss of sensation which one sees in a cortical lesion, that is involvement of the parietal lobe has more to do with the so-called gnostic sensation than the vital ones Thus pain, heat and cold are little affected if at all but stereognostic perception sense of position, spot localization the discrimination of the two points of a compass are involved *Vibratory sense* is not affected in cortical lesions *Dissociated sensory loss* occurs in syringomyelia where the lesion is usually in the central part of the cord A single lesion in this location will involve the fibers of pain, heat and cold which have entered by way of the posterior roots and are crossing The singling out of the functions of the posterior columns is seen in its most typical form in tabes and in the combined sclerosis of pernicious anemia, in which conditions position and vibration sensations are lost, while pain, heat, cold and touch are normal If pain sense is normal, heat and cold are likely to be so If position sense is normal, vibratory sense will likely be so, and if neither pain nor position senses are impaired, it will be unlikely that touch spot localization or stereognostic perception will be The ability of the individual to tell correctly numbers drawn on his skin by the examiner's finger, has been designated by Spiller as *graphesthesia* It goes with the gnostic sensibilities

It is always important to differentiate between hysteria and organic disease

Sensory loss in hysteria never corresponds to known anatomic distributions and is often bizarre and unusual The form of sensation most frequently lost in hysteria is pain This loss usually occurs after the patient has been examined by one or more physicians The part of the body which shows a loss of sensation will also often show loss of power or paralysis An extremity which presents a complete loss of power and sensation can have such findings if due to organic disease, only from a lesion of the peripheral nerves which go to that extremity If such were the case the extremity would show atrophy, loss of reflexes and reactions of degeneration findings which never occur in hysteria Paralysis of one side of the body if organic, may be accompanied by loss of all forms of sensation if the optic thalamus and internal capsule are involved but in such cases the deep reflexes will be increased ankle clonus and Babinski sign will be present and the abdominal reflexes lost on the side opposite the lesion Paralysis of one side of the body with loss of sensation due to hysteria will show no alteration of the reflexes neither deep nor superficial There often is deafness and blindness on the affected side and all forms of sensation are usually not equally involved

The deep reflexes are never lost in hysteria, but they may be hyperactive or exaggerated The superficial reflexes are normal and a pseudo ankle clonus may be present The pupillary reflex is not affected and the eye grounds are normal *Visual defects* in hysteria however are common especially the loss of panoramic vision or the occur

rence of the so called tubular vision Sudden loss of vision may occur in hysteria but may also be seen in certain toxic states such as nephritis in brain tumors and in multiple sclerosis The history of the illness will aid greatly in differentiating these forms of amaurosis Hysterical deafness may be detected by ear tests and also by the following reflex if a sudden noise is made beside a person whose hearing is normal the eyes blink If he is deaf from an organic cause no blinking would occur but if the deafness is due to hysteria the reflex arc being still intact the eyes will blink Casual conversation about an hysterically deaf person held in his presence may later on be repeated by him

Paralysis of a part of the body due to hysteria may simulate organic disease The reflexes are not altered the muscles are not atrophic the sensory loss is not according to anatomic distributions It must not be overlooked that hysteria may complicate an organic affection A patient who has had an organic paralysis may recover but an hysterical paralysis may ensue and prolong the illness Many cases of hysteria or functional nervous disorders are found in organic affections outside the nervous system especially in persons who are frightened by the physician and a bad prognosis given Atrophy of muscles fibrillary tremors reactions of degeneration pathologic reflexes fixed pupils, optic atrophy sensory loss according to known anatomic distributions and fever do not occur in hysteria

## Roentgenologic Studies

In recent years mechanical measures have been used extensively to aid in the diagnosis and the location of lesions especially tumors of the brain and spinal cord Dandy introduced the injection of air directly into the ventricles as a diagnostic procedure following this the practice of introducing air into the subarachnoid space by way of lumbar puncture was recommended these procedures are called ventriculography and pneumo-encephalography Whether ventriculography or encephalography should be done depends on the individual case If a brain tumor is undoubtedly present and cannot be accurately localized, ventriculography may be performed if a tumor is suspected encephalography may be cautiously performed The presence of papilledema and other signs of increased spinal fluid pressure are contraindications to encephalography An encephalogram should not be done in these cases in which a tumor of the posterior cranial fossa is suspected The procedure in doing an encephalogram is to remove 5 to 15 cc of fluid and to inject a corresponding amount of air This is repeated until from 100 to 150 cc of fluid have been removed and replaced with air Removal of such a large amount of fluid is a risky thing in brain tumors and should not be done routinely Both of these diagnostic measures are not without danger and death sometimes results from them Many of the patients are greatly shocked by either a ventriculogram or encephalogram

Angiography introduced by Moniz consists in the injection of a radiopaque substance (diodrast or thorotrast) into either the carotid or vertebral artery permitting *x* ray visualization of the cerebral vascular pathways It is useful in demonstrating aneurysms vascular malformations and sometimes tumors

To aid in the location of a spinal subarachnoid block such as is produced by a neoplasm pantopaque may be injected into the subarachnoid space either at the cistern magna or in the lumbar area As this substance is heavier than spinal fluid appropriate tilting of the patient on the fluoroscopic table will cause the oil to run up or down the spinal subarachnoid space

Any abnormalities present that impinge upon or block the column of radiopaque material may thus be seen fluoroscopically and films of course can be made as indicated Occasionally the oil may slip by a block and sometimes it is apparently arrested in its descent when no block exists It is wise to remove as much pantopaque as possible at the end of the procedure for if it is not removed it may remain in the spinal canal for years and rarely may produce signs of root irritation especially of the lower spinal roots In some cases a block in the spinal subarachnoid pathway may be vis

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Tests which should be done on the spinal fluid include those for total protein, globulin cell count with differentiation quantitative sugar Wassermann and colloidal gold test If evidence points to the possibility of meningitis a smear of the spinal fluid should be made and the fluid should be cultured A yellowish fluid (xanthochromia) may be due to a hemorrhage which has occurred in the subarachnoid space some days before it also occurs in the Froin syndrome The fluid may be actually bloody, due to blood in the subarachnoid space caused for example by spontaneous subarachnoid bleeding traumatic subarachnoid bleeding or rupture of a cerebral hemorrhage into the ventricles with escape into the subarachnoid space It may also be due to faulty technic If lumbar puncture is performed daily bloody spinal fluid due to subarachnoid hemorrhage will gradually become less and less bloody and within a week or ten days will be clear but yellow In another week or ten days the fluid will become normal Extradural bleeding does not cause a discoloration of the spinal fluid

Cells if present should be counted and their type determined An increase in cells is present in any inflammatory condition in the subarachnoid space such as neurosyphilis and meningitis An increase in cells is called pleocytosis The cells are frequently increased in epidemic encephalitis and in acute anterior poliomyelitis where the cells are first of the polymorphonuclear variety and then become lymphocytic in a few days at the most Eosinophilia of the spinal fluid usually means parasitic involvement of the central nervous system In cases in which meningitis or encephalitis is suspected quantitative tests for sugar should always be done In meningitis or any type except syphilitic the amount of sugar in the spinal fluid is diminished or absent whereas in a virus involvement of the nervous system the amount of sugar is occasionally slightly increased It is increased in diabetes depending on the blood sugar The chlorides in the spinal fluid are reduced in the various forms of meningitis but especially in the tuberculous form where they usually fall below 640 mg per 100 cc

*Colloidal gold Test* —A curve high to the left with fives and fours predominating has been called the paretic curve It was thought to be diagnostic of general paresis, it may occur however in almost any form of neurosyphilis in meningitis and in multiple sclerosis If the curve is high in the middle it has been referred to as the tabetic or meningitic curve and is frequently seen in neurosyphilis and meningitis Such a curve may also be seen in multiple sclerosis and in other organic affections of the nervous system especially acute inflammatory disease

The spinal Wassermann is an extremely important part of the examination of the spinal fluid Quantitative tests may be most helpful in evaluating the progress of treatment or the recrudescence of the disease

The estimation of the amount of *protein in the spinal fluid* is important The normal content is 15 to 45 mg per 100 cc The amount of protein in the spinal fluid is increased in fluid obtained below a block and it may also be increased in cerebral neoplasms Most infectious diseases of the nervous system and many degenerative ones at least some time during their course will show varying degrees of increased protein

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The value of information obtained from a lumbar puncture cannot be overemphasized In view of the great frequency with which neurosyphilis is associated with a negative blood Wassermann it is imperative that every patient showing organic involvement of the nervous system have an examination of the spinal fluid The only exception to this rule should be those cases in which the possibility of a brain tumor exists and then it is permissible to perform a lumbar puncture in order to estimate the pressure If this is high no fluid should be withdrawn There are many cases of vascular disease and of inflammatory reaction of the brain that are confused with tumor and low spinal

utilized following the injection of air into the spinal canal (air myelography)

The necessity of these mechanical aids to diagnosis is inversely proportional to the physician's clinical skill

### ELECTRO-ENCEPHALOGRAPHY

Berger (1929–1934) demonstrated that the human cortex possessed an electrical beat or rhythm, originating in the neurons, and devised suitable technical methods for its recording (electrical encephalography) This electrical activity of the cortex has been found to vary with age sensory stimulation sleep, and various changes in the physico chemical state of the body The electro-encephalogram therefore is of some value in demonstrating the presence of disturbed cortical function

At present, the greatest clinical value of electro-encephalography is in the detection of the paroxysmal cerebral dysrhythmia which is present in a certain percentage of epileptic cases It is also of some value in the localization of focal brain lesions, particularly those lying close to the surface such as tumors While various electro-encephalographic changes have also been found in many other neurologic and psychiatric diseases *the changes are in no sense* specific and therefore are of little help in exact clinical diagnosis

*Electro-encephalography* in some cases is a helpful diagnostic adjuvant when the electro-encephalographic findings are interpreted *in* connection with the clinical history and examination, and other laboratory findings but it should not be considered as an infallible diagnostic method whose use makes careful clinical study superfluous

### CEREBROSPINAL FLUID

Spinal fluid is usually withdrawn for examination at the level of the $L_3$–$L_4$ vertebræ The amount of fluid neccessary for examination is from 8 to 10 cc

Before any fluid is withdrawn in spinal cord cases jugular compression should be done in order to determine whether or not a spinal subarachnoid block exists This is the *Queckenstedt test* In the normal individual when the jugular veins are compressed with the spinal manometer in place, the pressure in the *spinal manometer rises* promptly and, on the release of pressure on the jugulars, falls suddenly If, however, there is a block in the subarachnoid space above the puncture, the pressure rises little or not at all on jugular compression and falls slowly and in a step-ladder fashion The conditions which may cause a block are spinal tumors diseases and injuries of the vertebræ such as Pott's disease, extradural abscess, inflammatory conditions in the meninges especially acute purulent meningitis adhesions and serous meningitis Syringomyelia occasionally produces a block either partial or complete If a complete subarachnoid block exists two chambers for the spinal fluid are formed and the fluid below the block undergoes definite changes The protein content is increased, supposedly due to venous transudation The point of block may be determined by the injection of pantopaque into the cisterna magna with the patient sitting *The oil will fall to the* point of block and can be seen by means of the roentgen ray The oil may also be injected into the lumbar space and, with the patient in the Trendelenburg position, it stops at the lowest end of the block In *tumors of the cauda equina the protein* content is increased the fluid may be yellowish and coagulate readily In thrombosis of the lateral sinus the Ayer-Tobey modification of the Queckenstedt test may give valuable information Under such a condition, compression of the jugular vein on the side of the lesion does not cause a rise of the fluid in the manometer whereas compression on the normal side causes an elevation *The Queckenstedt test is of value only in determining whether or not a block exists in the spinal subarachnoid pathway* It is of no value in cases in which only an intracerebral lesion is suspected and in such cases it should not be performed because of the danger of compressing the cerebellar tonsils and medulla into the foramen magnum causing death

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injury, which might impair the function of the roots In addition to Horner s syndrome which is present if the sympathetic rami are injured the small muscles of the hand and the flexors of the forearm are paralyzed Sensory disturbances are usually present and are limited to the ulnar side of the hand and forearm

### Erb Duchenne Paralysis

Upper brachial plexus palsy involving the fifth and sometimes the sixth cervical root is known as the Erb-Duchenne Paralysis It may occur as a birth injury as a result of a fall on the shoulder and occasionally following an anesthetic in patients in whom the arm has been abducted an externally rotated during the operation The paralyzed muscles include the biceps deltoid brachialis anticus supinator longus supra spinales infraspinatus rhomboids serratus magnus biceps latissimus dorsi and pectoralis major The arm hangs at the side and is internally rotated at the shoulder with the elbow extended and the forearm pronated Abduction and external rotation of the shoulders are lost the elbow cannot be flexed The biceps jerk is lost Movements of the wrist and fingers are unaffected Sometimes there is a small area of sensory loss over the deltoid In treatments the arm should be splinted with the shoulder abducted the elbow flexed and the forearm midway between pronation and supranation

### Landry s Paralysis

*Acute ascending paralysis* is a syndrome and not a disease Most instances of it are due to poliomyelitis disseminated encephalomyelitis and acute infectious polyneuronitis with cranial nerve symptoms The symptoms begin with flaccid paralysis of the feet and ascend rapidly and finally involve the bulb As a rule it produces death in three or four to ten days The paralysis is a flaccid one with loss of deep reflexes Sensation as a rule is not involved nor are the sphincters Atrophy is not seen because it does not have time to take place When the bulb is affected cranial nerve palsies may take place and death occurs from respiratory failure The treatment is supportive and the patient usually must be placed in a respirator

### Meniere s Syndrome

Due to an affection of the semicircular canals and the auditory nerve the three symptoms which make up this syndrome are deafness dizziness and tinnitus Nausea vomiting and sweating are secondary symptoms The condition may begin abruptly or may be a slowly progressive affair depending upon the etiologic factor Usually it occurs in the form of attacks An attack may come on suddenly with vertigo so severe that the patient drops as though struck Rarely he may be momentarily unconscious so that the diagnosis of epilepsy is considered Due to the intense dizziness he becomes nauseated vomits and breaks out in a cold perspiration and occasionally has diarrhea He is afraid to move because of dizziness which he fears may be increased by movement The acute attack may last from a few minutes to a few days The frequency of the attacks varies greatly

The pathology of the syndrome is obscure Toxemias intoxications syphilis malaria and occasionally tumor in the angle may produce the symptoms of Meniere s syndrome

The treatment must be directed to the cause Intracranial section of the vertibular branch of the eighth nerve has been suggested in those cases in which total deafness is present and intense vertigo still persists Bromide and luminal may cut down the frequency and severity of the attacks while investigation as to the cause is under way Some cases have been reported as being benefited by the intravenous injection of histamine (Horton) Talbott and Brown suggest the daily administration of 6 to 10 grams of potassium chloride given as a 25 per cent aqueous solution along with a diet low in sodium Nicotinic acid and thiamin hydrochloride may be helpful in some cases

## NEUROSYPHILIS

*Introduction* —Syphilis of the nervous system includes luetic diseases of the blood vessels of the brain and cord Syphilis rarely affects the peripheral nervous system The symptoms of neurosyphilis usually manifest themselves from five to fifteen years after the initial lesion However they may occur while the patient has the secondary rash or may be delayed thirty to forty-five years vascular neurosyphilis in particular may occur in the first years of the

pressure may be of great importance in helping to clear the diagnosis On the other hand it must be remembered that the spinal fluid pressure may be increased in some brain lesions of a non space taking nature as well as in patients who are tense during the procedure of lumbar puncture In patients obviously suffering from a brain tumor—a lumbar puncture is not needed for diagnostic purposes, but where the disks are normal and the symptoms and signs are nonconclusive it is advisable The great frequency of general paresis, and the many ways in which it may become manifest clinically makes it imperative that the spinal fluid be examined in every mental case and also in every patient suffering from what seems to be a psychoneurosis In arriving at the diagnosis of a patient in coma, an examination of the spinal fluid is as necessary and urgent as an investigation of the urine and blood

To avoid a headache following lumbar puncture, a narrow gauge needle should be used and the patient should be kept in bed with the head low for twenty four hours Fluids should be forced In some cases the incidence of postpuncture symptoms may be reduced by giving sodium amytal, gr 3 (0 2 gm ) prior to the procedure As little fluid should be removed as is necessary for the tests If the headache does occur it may last from a day to three or four weeks The headache is often accompanied by a pain in the neck, between the shoulders dizziness and even vomiting One cc of obstetrical pituitrin given hypodermically may relieve the distress or forty cc of sterile distilled water or 100 cc of a hypotonic sterile salt solution given intravenously may also be of benefit

## NEUROLOGIC SYNDROMES

Certain syndromes which will frequently be referred to under the name of the individuals who first described them are given below

### Brown-Sequard s Syndrome

This syndrome is due to a unilateral lesion of the cord It is caused by an injury such as those inflicted by stab or bullet wounds by disease, especially syphilis and by spinal tumors If one half of the cord at a distinct level is completely destroyed, the symptoms will be as follows paralysis of the spastic type with pyramidal tract and posterior column signs on the side of the lesion and below it, and anterior horn symptoms at the level of the lesion There may also be disturbance in all forms of sensation at the level of the lesion On the opposite side and below there will be loss of pain heat and cold and, in some cases, of touch and deep pressure In nontraumatic disorders it is rare to see a complete hemisection of the spinal cord

### Horner s Syndrome

This is a paralysis of the cervical sympathetic and results in the following symptoms enophthalmos which is due to paralysis of the non striated orbital muscle of Muller, miosis—the cervical sympathetic dilates the pupil and, if this function is paralyzed, the constrictor supplied through the third nerve functions unopposed and produces a small pupil The pupil does not dilate normally when shaded but contracts quickly to light and in convergence Narrowing of the palpebral fissure is due to paralysis of the non striated part of the levator palpebræ and also to the fact that, as the eyeball is retracted, the lids come closer together Vasomotor signs may also occur and the intraocular tension is diminished on the affected side Instillation of 2 per cent cocaine solution fails to dilate the pupil Furthermore stimulation of the side of the neck on which the paraly is exists does not produce dilatation of the pupil which it normally should do This is the ciliospinal reflex The disturbance of sweat secretion may be brought out by injection of pilocarpin Cervical sympathic paralysis may occur from lesions of the medulla such as syringobulbia and occlusion of the posterior inferior cerebellar artery by lesions within the cord and also by involvement of the eighth cervical or first thoracic root especially the latter and the ascending fibers of the cervical sympathetic in the neck The latter are frequently injured in operations of the neck

### Klumpke s Paralysis

A paralysis of the lower roots of the brachial plexus which is due to lesions which involve the nerves derived from the seventh and eighth cervical and the first dorsal roots The roots may be torn by a dislocated shoulder or efforts at reduction It may also be due to efforts at delivery especially breech births and also to any condition such as cervical rib, tumor syphilis or

injury, which might impair the function of the roots In addition to Horner s syndrome which is present if the sympathetic rami are injured the small muscles of the hand and the flexors of the forearm are paralyzed Sensory disturbances are usually present and are limited to the ulnar side of the hand and forearm

### Erb Duchenne Paralysis

Upper brachial plexus palsy involving the fifth and sometimes the sixth cervical root is known as the Erb-Duchenne Paralysis It may occur as a birth injury as a result of a fall on the shoulder and occasionally following an anesthetic in patients in whom the arm has been abducted an externally rotated during the operation The *paralyzed muscles include the biceps deltoid* brachialis anticus supinator longus supra spinales infra pinatus rhomboids serratus magnus biceps latissimus dorsi and pectoralis major The arm hangs at the side and is internally rotated at the shoulder with the elbow extended and the forearm pronated Abduction and external rotation of the shoulders are lost the elbow cannot be flexed The biceps jerk is lost Movements of the wrist and fingers are unaffected Sometimes there is a small area of sensory loss over the deltoid In treatments the arm should be splinted with the shoulder abducted the elbow flexed and the forearm midway between pronation and supranation

### Landry s Paralysis

*Acute ascending paralysis* is a syndrome and not a disease Most instances of it are due to poliomyelitis disseminated encephalomyelitis and acute infectious polyneuronitis with cranial nerve symptoms The symptoms begin with flaccid paralysis of the feet and ascend rapidly and finally involve the bulb As a rule it produces death in three or four to ten days The paralysis is a flaccid one with loss of deep reflexes Sensation as a rule i not involved nor are the sphincters Atrophy is not seen because it does not have time to take place When the bulb is affected cranial nerve palsies may take place and death occurs from respiratory failure The treatment is supportive and the patient usually must be placed in a respirator

### Meniere s Syndrome

Due to an affection of the semicircular canals and the auditory nerve the three symptoms which make up this syndrome are deafness dizziness and tinnitus Nausea vomiting and sweating are secondary symptoms The condition may begin abruptly or may be a slowly progressive affair depending upon the etiologic factor Usually it occurs in the form of attacks An attack may come on suddenly with vertigo so severe that the patient drops as though struck Rarely he may be momentarily unconscious so that the diagnosis of epilepsy is considered Due to the intense dizziness he becomes nauseated vomits and breaks out in a cold perspiration and occasionally has diarrhea He is afraid to move because of *dizziness which he fears may be increased* by movement The acute attack may last from a few minutes to a few days The frequency of the attacks varies greatly

The pathology of the syndrome is obscure Toxemias, intoxications syphilis malaria and occasionally tumor in the angle may produce the symptoms of Meniere s syndrome

The treatment must be directed to the cause Intracranial section of the vertibular branch of the eighth nerve has been suggested in those cases in which total deafness is present and intense vertigo still persists Bromide and luminal may cut down the frequency and severity of the attacks while investigation as to the cause is under way Some cases have been reported as being benefited by the intravenous injection of histamine (Horton) Talbott and Brown suggest the daily administration of 6 to 10 grams of potassium chloride given as a 25 per cent aqueous solution along with a diet low in sodium Nicotinic acid and thiamin hydrochloride may be helpful in some cases

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infection The effect of the spirochetal involvement of the nervous system is widespread, and while the location of the syphilitic process in a particularly vital spot may lead to disabling symptoms examination of other parts of the cord and brain in such a patient will reveal the fact that the disease has not been entirely localized One of the commonest manifestations of neurosyphilis is tabes dorsalis In this disease the pathology which accounts for the disabling symptoms in the lower extremities exists in the lumbo-sacral part of the cord, yet a considerable syphilitic process may and usually does, exist at the base of the brain in addition Why certain people with syphilis never develop disease of the nervous system is not known There is some evidence, but not entirely proved, that there may be a special neurotrophic strain of spirochetes with a predilection for the nervous system Conjugal neurosyphilis which is not infrequent, lends strength to the theory that a special strain of spirochetes exists Others believe that the occurrence of neurosyphilis depends upon the constitution of the individual Some believe that given a patient with syphilis, overwork, worry trauma and especially the excessive use of alcohol predispose to the occurrence of neurosyphilis It is certainly true that alcohol and syphilis do not mix well and the excessive use of the drug is a common point in the history of neurosyphilis It has been estimated that about 10 per cent of the patients in the hospitals for the mentally ill are there because of paresis or dementia caused by syphilis

*Types of Neurosyphilis* — Neurosyphilis is divided into the meningeal parenchymatous vascular and meningovascular types An isolated gumma or syphiloma is rare, although gummatous meningitis is common The syphilitic meningitis may occur at any part of the cerebrospinal axis but is particularly common in the region of the optic chiasm, in the interpeduncular space and in the cerebellopontine angle It also occurs in the spinal cord especially on the dorsal aspect The meninges are infiltrated with round and plasma cells The parts of the central nervous system beneath the involved meninges show evidence of inflammatory reaction in such cases the process may be referred to as meningoencephalitis and meningomyelitis Hypertrophic pachymeningitis usually found in the cervical cord consists of great thickening of the dura and is usually, but not always, due to syphilis This process leads to rim degeneration of the cord atrophy of the roots and involvement of the vessels which nourish the cord As a result, cavitation in the central parts of the cord often occurs

The two forms of neurosyphilis which are examples of the parenchymatous type are general paresis and tabes dorsalis Pathologically, general paresis is a syphilitic meningoencephalitis characterized by a fibrous thickening and infiltration of the meninges with round cells of the lymphocytic and plasma type In the cortex the findings are a breaking up of the cyto architecture independent of the vascular supply, perivascular infiltration with cells identical with those of the pia the occurrence of rod cells in great number and new vessel formation By means of special staining methods it is possible to detect the increase of iron and enormous numbers of so-called Hortega and Cajal cells of the glial type A certain percentage of cases probably not over 15, have sclerosis of the posterior columns of the cord and the usual syphilitic meningitis, producing the clinical picture that is commonly called taboparesis Remissions either spontaneous or as a result of therapeutic measures may bring about decided improvement in the pathologic picture Tabes is an affection of the posterior roots posterior ganglia and the meninges covering the dorsal aspect of the cord with secondary changes in the posterior columns Whether the lesion is primarily in the roots or the meninges has not been settled satisfactorily Very rarely in tabes the anterior roots and the anterior horn cells may be involved Basilar meningitis usually exists in tabes and accounts for the cranial nerve symptoms

In vascular syphilis the syphilitic process is found in the blood vessels more particularly in the arteries The muscular and elastic fibers are infiltrated with lymphocytes The walls of the vessels especially the intima are ultimately involved with the

formation of a thrombus in the vessels An artery may also be the site of an aneurysm although syphilis is not a common cause of aneurysm of the cerebral vessels If an artery is completely thrombosed or if it ruptures as the result of aneurysm cerebral softening or cerebral hemorrhage results

The relation of trauma to syphilis of the nervous system is an important one Trauma of course cannot produce neurosyphilis but it can bring out its symptoms or aggravate them The question of relationship between trauma and syphilis has a very direct medico legal significance

## GENERAL PARESIS

*Synonyms* —General paralysis of the insane dementia paralytica

*Introduction* —Among the various forms of mental disease there is none which may start in such a variety of ways and exhibit such a protean symptomatology as general paresis It has been known for a long time that the initial symptoms of paresis are often similar to those of the psychoneuroses the onset may also be with excitement depression or a paranoid trend Irritability, nervousness, bradyphrenia and other common neurophsychiatric complaints are among some of the frequent early symptoms

Paresis is a common mental disease making up about 10 per cent of those in mental hospitals and may masquerade under such different guises that it should always be thought of in any psychiatric disturbance occurring between the ages of twenty five and seventy years furthermore juvenile paresis is common enough in the psychoses of childhood

From a diagnostic standpoint too much stress has been laid upon the grandiose form of paresis and too little upon the other and more common ways in which the disease asserts itself Once general paresis is in full bloom with changes in character delusions of grandeur physical signs and mental deterioration a tyro can or at least should make the diagnosis with facility

*Symptoms* —All psychoneurotic manifestations should be considered as potentially due to paresis This is particularly so if these symptoms have come on in a male between the ages of twenty five and forty years without a history of previous attacks Mental symptoms which initiate syphilis may be those of excitement or depression the patient may simulate manic depressive insanity in either phase Ideas of grandeur especially in regard to strength and wealth are common but many diagnoses of paresis will be missed early if the physician waits for the appearance of ideas of grandeur Memory is impaired and judgment is affected in all lines This leads the paretic into difficulties especially in regard to alcohol and sex He becomes loose in his manner of dress and in his talk Because of lack of attention and loss of memory he loses interest in or ruins his business he forgets important appointments He often orders or buys an unwarranted amount of materials While the paretic is usually happy and euphoric he is also given to outbursts of temper and is frequently unmanageable While not usually suspicious the paretic may become extremely paranoid He rarely attempts suicide but may become assaultive especially if his aims are interfered with Some of the cases will pursue a course which runs into a state of simple dementia with mental dilapidation

In some cases mental symptoms are initially minimal or absent and the disease is ushered in by the occurrence of hemiplegia aphasia or convulsions These neurologic symptoms are often transient subsiding spontaneously within a few days

*Signs* —The physical signs of paresis are important and many of them are found in most cases The speech is of a tremulous slurred dysarthric variety and is made much worse if the patient drinks alcohol Test phrases such as Methodist Episcopal Hospital The Royal Riding Artillery Brigade and ' Peter Piper picked a peck of pickled peppers are said with difficulty The lips tongue and fingers show a distinct simple tremor The face has more or less of a masked expression The pupils are often of Argyll Robertson type but many cases of what might be considered early paresis will not show changes in the pupils and if possible the diagnosis should be made before they occur and before the presence of delusions of grandeur Ocular palsies and optic atrophy may be seen but are not as common

as they are in other forms of neurosyphilis All of the deep reflexes, because of cortical involvement, are increased but it is rare that ankle clonus or Babinski's sign appears The handwriting shows a tremor is carelessly done and letters words and even sentences may be left out when the patient writes from dictation If the posterior columns are affected Romberg's sign and a loss of the deep reflexes may be detected Paralytic attacks (hemiplegia monoplegia, aphasia) status epilepticus and partial continuous epilepsy may occur in the course of paresis The paralytic phenomena may disappear as quickly as they appeared Many of the patients become bedfast, emaciated develop infections in the urinary system have bed sores and finally die of pneumonia, tuberculosis or status epilepticus

*Laborlory Findings* —Examinations of the blood and spinal fluid are of great aid in the diagnosis of paresis In untreated patients practically 100 per cent will have a positive spinal fluid Wassermann The cell count may vary In a series of cases of ours it ranged from 1 to 400, the average being 31 Almost every untreated patient will show alteration in the colloidal-gold curve, such as 5555543321 fives and fours should predominate in the reading of the first 4 to 6 tubes The globulin is increased It must be remembered that cases of diffuse neurosyphilis non paretic in type can produce in the spinal fluid changes almost exactly similar to those of paresis The finding therefore, of a 4 plus Wassermann an increase in the cells and a colloidal gold curve of the paretic curve in the spinal fluid is not enough on which to base the diagnosis of ' general paresis The blood Wassermann is positive in 95 to 100 per cent of untreated patients If a case is supecteds to be one of general paresis has not received anti syphilitic treatment and the blood and spinal fluid are negative for syphilis, such an individual will usually be proved to have a brain tumor arteriosclerosis, chronic alcoholism, pernicious anemia or pellagra Multiple sclerosis frequently shows an alteration of the colloidal gold curve at some stage of the paretic type, but the Wassermann of the blood and the fluid are negative and there is no increase of cells

Before the advent of fever therapy the *prognosis* in paresis was very bad practically all cases dying within three years Since fever therapy, tryparsamide bismuth and penicillin have been used, more than 50 per cent of the cases do well and the span of life of the remaining is usually greatly increased

The *diagnosis* of paresis should be made as early as possible The frequency of the disease and the various ways in which it may begin make it imperative that every psychotic individual be examined physically and from the laboratory standpoint for syphilis Chronic alcoholism drug poisoning by such compounds as barbital frontal tumors pellagra, arteriosclerosis and multiple sclerosis may sometimes be mistaken for general paresis Occasionally the mental symptoms produced by pernicious anemia are similar to those of paresis It is in such instances that the laboratory is of great aid in ruling out the presence of syphilis Diffuse neurosyphilis especially that characterized by bilateral lesions either of softening or of gumma may produce a group of symptoms and laboratory findings that are almost indistinguishable from those of general paresis Hallucinations as a rule do not occur in paresis unless the patient is in addition an alcoholic Sometimes a patient with dementia precox, especially one of the paranoid type acquires syphilis and later develops neurosyphilis in such conditions hallucinations may be present

*Treatment* —The important considerations in the handling of a case of paresis are the protection of the patient the treatment of the underlying condition and if necessary the appointment of a guardian to handle his affairs and money The last used to be of great importance and remains so if the mental symptoms are severe The addition of penicillin to the treatment of paresis has however hastened the return of many paresis patients to normal productive lives Most paretics should be admitted to a mental hospital although many may be handled in a general one

The most important therapeutic procedures in the treatment of paresis are peni

cillin and fever therapy Some writers have expressed the opinion that penicillin alone is sufficient In our experience however fever therapy and penicillin together constitute the best treatment Every patient with general paresis if under 60 years of age and without serious medical complications *should receive fever therapy as soon as* possible Fever therapy was first used by Wagner von Juaregg who employed malaria as the source of the fever A diabetic may be carried through a course of fever with certain added precautions The same is true for a patient with tuberculosis Severe cardiacs react poorly to fever Nephritis is a contraindication to malaria or fever induced by killed typhoid organisms but a nephritic may be given fever cautiously in the Kettering hypertherm Patients with moderate or severe anemias should not be given malaria or typhoid vaccine but may receive fever in the hypertherm

Malaria in our opinion is the best state for fever therapy It is the most comfortable type of fever to endure no expensive machinery is required less nursing care is needed and it undoubtedly gives the best results The disadvantages are the incubation period involved which may vary in length from 5 days to 5 weeks or longer the indefiniteness of the time of the chill and following fever the lack of general availability of malaria and the progressive weight loss and the anemia that usually develop To state briefly 8 to 10 cc of blood taken preferably during a chill from a known case of malaria (tertian or quartan type) is given intravenously to the case under treatment (incompatibility of bloods may be overlooked) He should be allowed to have a total of 50 to 70 hours of fever over 103° (the temperature is orally taken) During the course of treatment the patient s physical condition should be checked daily and estimations of the hemoglobin and blood urea nitrogen should be made not less than twice weekly Termination of the malaria is indicated in the presence of rapidly increasing anemia a substantial increase in the blood urea nitrogen a high fever prolonged for more than 24 hours or signs of generalized collapse In some cases a rest period is all that is required to allow the patient to recuperate In such cases, thiobismal 0 1 to 0 2 grams given intramuscularly will usually stop the fever for 7 to 14 days If this drug is not effective or the malaria is to be completely terminated then quinine atabrine chlorguanide hydrochloride or chloroquin in appropriate dosage *is recommended* It should be *mentioned* here that penicillin may be given concurrently with malaria in the usual antisyphilitic doses it has no effect on the plasmodium Arsenicals and heavy metals should not be given during a course of malarial fever therapy

In patients unsuitable for malaria the Kettering hypertherm may be used Its advantages are that a few patients not medically suitable for malaria may be successfully carried through a course of fever One knows the time of the fever and how long it will last Patients especially negroes who will not take malaria may be given the hypertherm

A third type of fever is that induced by killed typhoid organisms Practically its only advantage in our opinion is that typhoid vaccine is usually available in all hospitals

To summarize it is our opinion that malaria is the best type of fever therapy for paretics the Kettering hypertherm is a good second and a most useful addition to a ward in which malaria is used Killed typhoid organisms should be used only if one of the other two are not available Patients should be well studied medically but the responsibility rests with the neurologist as to the choice of patients for fever The first responses from fever therapy may be noted after 10 to 20 hours and improvement usually continues rapidly for 3 to 6 months The full benefit may not be obtained for a year or more A second or third course of fever may be given as indicated

As mentioned above penicillin may be given at any time in relation to fever therapy It is our opinion that as soon as the diagnosis of paresis is established penicillin should be started A minimum of 10 million units should be given intramuscularly over a 10 to 15-day period Aqueous penicillin 100 000 units every 3 hours day and night for 100 injections (12½ days) crystacillin 300 000 units every 8 hours for 34 injections

a procaine penicillin in aluminum monostearate base, 900,000 units once daily for 12 days—these are suggested schedules.

Because of the mental symptoms, paretics are frequently subjected to electroconvulsive therapy. Generally speaking such treatment is to be condemned. We have recently read reports in which the authors advocated the use of electroshock as the sole treatment for paresis. The patients we have seen so treated may have been improved mentally for short periods of time, but all cases observed by us became very much worse within a few weeks and when the correct therapies were instituted did not do so well as might have been expected. Electroshock, however, does have a place in the management of paresis. Early in the course of fever and penicillin therapy it should be reserved for those episodes in which the patient becomes acutely excited, otherwise unmanageable or does not eat. Then and only if utterly necessary, a paretic should be given daily EST for 2 or 3 days. Later in the course of treatment, after fever has been completed and adequate penicillin has been given and the patient has not been making reasonable progress mentally, a series of electroshocks may be cautiously tried.

Unless the patient is markedly deteriorated on admission there will usually be sufficient improvement after fever and penicillin are completed for the patient to be discharged from the hospital. We believe that a paretic, or any patient suffering from luetic involvement of the central nervous system, should be followed for the rest of his natural life. Blood and spinal fluid tests on patients discharged after the above treatments are performed at monthly intervals for 3 months, then at quarterly intervals for the remainder of the first year. Thereafter such tests are done as indicated, usually at 4-, 6-, or 12-month intervals. Indications for out-patient treatment are inadequate treatment as an in-patient, not sufficient improvement clinically as an in-patient, progress of the disease or recurrence of signs and symptoms, marked increase in either blood or spinal-fluid titres. Drugs used in the further treatment of paresis have been tryparsamide, bismuth, mercury and iodides. The latter two are not used much at present and tryparsamide and bismuth may be supplanted by penicillin although tryparsamide is toxic to many paretics. Bismuth subsalicylate in oil may also be used. The injections are given intramuscularly, usually in the buttocks. The dose is 0.260 grams; a course of treatment, again, may last 16 weeks. Courses may be repeated after 2- to 4-week rest periods.

With the advent of the longer-acting depot penicillins we have done much experimental work with these drugs in the out-patient care of paresis. Though too early to give definite results, they do show great promise. At this writing we are using 5 cc. (1.5 million units) of a procaine penicillin in aluminum monostearate base weekly for 10 weeks as a single course of therapy. The only complication has been an occasional allergy which is usually controlled by antihistaminics. The place of aureomycin and other newer antibiotics has not yet been established in the therapy of paresis.

It sometimes becomes obvious that out-patient therapy is not adequate, that the patient is slipping and should be readmitted for further therapy (fever). In selected cases it has been possible to give fever therapy (Kettering hypertherm) on an out-patient basis.

In addition to fever, penicillin, *et al.*, it must be remembered to treat the individual as a human being, one who is sick with a chronic potentially devastating infection. Proper diet, rest, vitamins, freedom from fear and worry, the appointment of a guardian if deemed necessary and the absolute avoidance of alcohol are additional measures.

If an individual does not respond to adequate therapy, he should be resurveyed and the possibility of another disease, such as tumor, investigated.

## TABES DORSALIS

*Synonyms.*—Locomotor ataxia. Posterior spinal sclerosis.

*Symptoms.*—Tabes dorsalis is always due to syphilis, but there is a pseudotabes usually due to multiple neuritis with loss of deep sensation and caused by such conditions as diabetes and diphtheria, which may be mistaken for real tabes. As a rule five to

fifteen years elapse after syphilis has been acquired before the symptoms of tabes ensue However the writers have seen a case of tabes dorsalis bedridden because of ataxia fourteen months after the initial lesion Probably the commonest early symptom is pain which usually appears in the lower extremities in the buttocks and about the the abdomen The pain of tabes may occur in the chest in the upper extremities or in the distribution of the fifth nerve It has been described as a boring lancinating pain and patients have said that the pain feels as though it were produced by a knife stuck into the flesh and turned around It comes out of a clear sky and may last for a few moments hours or days If the symmetrical roots are involved the patient has a *girdle sensation* Occasionally pressure on the painful area will relieve the pain but not infrequently the area is as tender as though the patient had multiple neuritis The pains have a tendency to occur in spots the patient describes these spots as though they contained a thousand toothaches and could be covered with a dime or quarter The pain is mistaken for neuritis arthritis phlebitis acute abdominal conditions, pleurisy angina pectoris and hysteria

The next important group of symptoms are those referable to the functions of the conus Most common of these is the *disturbance in the control of the bladder* resulting in retention of urine incontinence and difficulty in passing it Any of these symptoms appearing in an adult for the first time hould arouse suspicion of syphilis of the nervous system Loss of control of the rectal sphincter is occasionally seen but more often constipation occurs Diminished or lost libido is also a symptom frequently complained of and is due to involvement of the lowest part of the cord Symptoms referable to *the cranial nerves* are next in importance Diplopia dimness of vision deafness bilateral facial palsy in fact any of the cranial nerves may be involved by the syphilitic meningitis which is so common at the base in cases of tabes dorsalis *Gastric crises* and other forms of crises are frequent and are seen in their worst form in the patients who have lancinating pains The usual form of crisis is a gastric one which like a lancinating pain may strike with lightning rapidity It is characterized by extreme pain in the abdomen and vomiting It may last for hours, or days and cause marked reduction in weight and severe dehydration of the patient The extremes of crises may vary from a mild affair to one which makes life unbearable The exact manner in which a crisis is produced is not known It is also needless to say that this is the type of patient who may be subjected to exploratory laparotomies Gastric and intestinal studies in these cases are normal Crises referable to the intestines rectum larynx and vision may be observed Paresthesias in the feet and especially along the ulnar borders of the hands and forearms may be early symptoms

Ataxia is not an early symptom It is due to changes in the posterior columns It is most noticeable to the patient when he walks in the dark or with his eyes closed *Trophic conditions* may be the first to be observed by the patient but as a rule are late in appearing The commonest trophic disorders are perforating ulcers found on the soles and Charcot joints which usually affect the hips knees and ankles The lumbosacral spine is not an infrequent site for Charcot joints

*Physical Signs* — When the patient is examined the following signs may be detected in the order of their importance and onset (1) loss of the deep reflexes especially the Achilles and the patellar The biceps and triceps are not involved early unless the patient has cervical tabes (2) pupillary abnormalities (3) cranial nerve signs including palsies deafness and optic atrophy (4) disturbance of pain sense in the areas in which the patient has pain this form of sensation is disturbed earliest in tabes much before vibration and position (5) ataxia of station and gait and ataxia in the upper extremities and (6) trophic disorders especially Charcot joints and perforating ulcers

The deep reflexes are lo t because of interruption of the reflex arc While the patellar reflexes are u ually the ones tested it is of equal importance to determine the Achilles reflexes as they may be the first to be lost The skin reflexes are not altered unless there

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*Synonyms* —Locomotor ataxia Posterior spinal sclerosis

*Symptoms* — Tabes dorsalis is always due to syphilis but there is a pseudotabes usually due to multiple neuritis with loss of deep sensation and caused by such conditions as diabetes and diphtheria which may be mistaken for real tabes As a rule five to

fifteen years elapse after syphilis has been acquired before the symptoms of tabes ensue However the writers have seen a case of tabes dorsalis bedridden because of ataxia fourteen months after the initial lesion Probably the commonest early symptom is pain which usually appears in the lower extremities in the buttocks and about the the abdomen The pain of tabes may occur in the chest in the upper extremities or in the distribution of the fifth nerve It has been described as a boring lancinating pain and patients have said that the pain feels as though it were produced by a knife stuck into the flesh and turned around It comes out of a clear sky and may last for a few moments hours or days If the symmetrical roots are involved the patient has a *girdle sensation* Occasionally pressure on the painful area will relieve the pain but not infrequently the area is as tender as though the patient had multiple neuritis The pains have a tendency to occur in spots the patient describes these spots as though they contained a thousand toothaches and could be covered with a dime or quarter The pain is mistaken for neuritis arthritis phlebitis acute abdominal conditions pleurisy angina pectoris and hysteria

The next important group of symptoms are those referable to the functions of the conus Most common of these is the *disturbance in the control of the bladder* resulting in retention of urine incontinence and difficulty in passing it Any of these symptoms appearing in an adult for the first time should arouse suspicion of syphilis of the nervous system Loss of control of the rectal sphincter is occasionally seen but more often constipation occurs Diminished or lost libido is also a symptom frequently complained of and is due to involvement of the lowest part of the cord Symptoms referable to *the cranial nerves* are next in importance Diplopia dimness of vision deafness bilateral facial palsy in fact any of the cranial nerves may be involved by the syphilitic meningitis which is so common at the base in cases of tabes dorsalis *Gastric crises* and other forms of crises are frequent and are seen in their worst form in the patients who have lancinating pains The usual form of crisis is a gastric one which like a lancinating pain may strike with lightning rapidity It is characterized by extreme pain in the abdomen and vomiting It may last for hours, or days and cause marked reduction in weight and severe dehydration of the patient The extremes of crises may vary from a mild affair to one which makes life unbearable The exact manner in which a crisis is produced is not known It is also needless to say that this is the type of patient who may be subjected to exploratory laparotomies Gastric and intestinal studies in these cases are normal Crises referable to the intestines rectum larynx and vision may be observed Paresthesias in the feet and especially along the ulnar borders of the hands and forearms may be early symptoms

Ataxia is not an early symptom It is due to changes in the posterior columns It is most noticeable to the patient when he walks in the dark or with his eyes closed *Trophic conditions* may be the first to be observed by the patient but as a rule are late in appearing The commonest trophic disorders are perforating ulcers found on the soles and Charcot joints which usually affect the hips knees and ankles The lumbosacral spine is not an infrequent site for Charcot joints

*Physical Signs* —When the patient is examined the following signs may be detected in the order of their importance and onset (1) loss of the deep reflexes, especially the Achilles and the patellar The biceps and triceps are not involved early unless the patient has cervical tabes (2) pupillary abnormalities (3) cranial nerve signs including palsies deafness and optic atrophy (4) disturbance of pain sense in the areas in which the patient has pain this form of sensation is disturbed earliest in tabes much before vibration and position (5) ataxia of station and gait and ataxia in the upper extremities and (6) trophic disorders especially Charcot joints and perforating ulcers

The deep reflexes are lost because of interruption of the reflex arc While the patellar reflexes are usually the ones tested it is of equal importance to determine the Achilles reflexes as they may be the first to be lost The skin reflexes are not altered unless there

be a distinct loss of sensation in the distribution of the reflexes.

The same pupillary signs may occur in tabes as in other forms of syphilis. They may vary in size from pin point to wide dilatation, the inequality may be slight but the patient may have one pin point and one widely dilated pupil. The pupils are usually irregular, react sluggishly and, as the disease progresses, lose their reaction to light. The reaction to accommodation is preserved early (Argyll Robertson phenomena), but in an advanced case of tabes the pupils may be fixed. Occasionally the so called paradoxical reaction occurs in which the pupils dilate instead of reacting to light.

Any of the motor cranial nerves may be implicated but those which are commonly affected are the third and sixth. Bilateral seventh nerve palsy, especially if it is accompanied by bilateral eighth nerve symptoms, is usually due to syphilis. Optic atrophy in some degree is a frequent sign if it is looked for.

The common loss of sensation in tabes dorsalis is for pain. If the patient is seen early enough and tested for sensation it will usually be found that all forms of sensation are preserved except pain sense which is diminished, retarded or lost in the area in which the patient complains of pain or in a spotty distribution in the lower extremities. When ataxia becomes evident, position and vibration senses are disturbed.

Ataxia in station is called the *Romberg sign*. The patient standing with his feet together and with his eyes closed will sway abnormally if his sense of position is involved, and this is what finally happens in the tabetic. His gait is ataxic for the same reason; he throws the feet far, brings the heels down in a stamping manner; the feet are likely to be more widely separated than usual and the knees are hyperextended because of hypotonia and relaxation of the joints and tendons. Early ataxia in gait may be brought out by having the patient walk a "chalk line," by having him walk with his eyes closed or by walking backward. The patient himself complains that he walks poorly in the dark. The test for ataxia in the upper extremities is the finger to nose test and in this the patient with involvement of the cervical cord cannot accurately place his index finger on the tip of his nose with the eyes closed.

The joint most frequently the site of a Charcot joint (arthropathy) is the knee (*See Chapter 28*). Perforating ulcers usually occur on the soles of the feet. They are deep painless affairs and difficult to cure. Localized atrophy of the muscles occasionally occurs in tabes. A more common symptom is for the muscular system to become generally soft, flabby and underdeveloped. It is rare that one sees a fat tabetic.

Cystoscopic examination will reveal a 'cord' bladder.

*Laboratory Findings.*—The spinal fluid Wassermann is positive in 60 to 90 per cent of the untreated cases. The blood Wassermann is positive in approximately 50 per cent of the untreated cases. The cells of the spinal fluid are increased and may vary in number from 10 to 200 or 500 with an average of 30 to 75. The colloidal gold curve test shows an alteration to the left and in the middle such as 1223100000. Occasionally in tabes a stronger colloidal gold reaction may be found even of the paretic type.

The *diagnosis* of tabes should be made before marked physical signs present themselves. Pain, bladder disturbance and cranial nerve symptoms point directly to syphilis of the nervous system and most likely tabes. The diagnosis should be made before ataxia occurs. Tabes may be confused with the pseudotabetic form of multiple neuritis and with the combined sclerosis of pernicious anemia. The juvenile type of tabes due to congenital syphilis may be confused with Friedreich's ataxia or with a cerebellar tumor. Adie's syndrome may be confused with tabes dorsalis. It is a nonluetic condition characterized by tonic pupils and absent tendon reflexes. It usually occurs in young persons, especially females. One or both pupils may be affected. The typical tonic pupil has been previously described in the section on the third nerve. The pupillary disturbances may occur without reflex loss and conversely. The condition is benign and its cause is as yet undetermined. Negative serologic findings and the absence of the other signs and symptoms of tabes aid in its differentiation.

The course of tabes is usually slowly progressive but there are some cases which run a rapid course and the patients become bedfast or chairfast but then live on for years

*Treatment* —The patient should be placed in the best possible general health, his diet and mode of living made ideal alcohol tobacco and excesses of all sorts forbidden and plenty of sunshine, fresh air and rest prescribed He should not be permitted to take long walks to work until he is exhausted or to become overfatigued Massage and re-education of the ataxic extremities greatly benefits the tabetic Attacks of pain and crises may be relieved by analgesic drugs The signs once manifested rarely disappear under treatment For specific treatment *see* Chapter 3

### Other Forms of Neurosyphilis

In addition to paresis and tabes dorsalis syphilis may produce meningomyelitis myelitis Brown-Sequard s paralysis meningo-encephalitis bilateral cerebral lesions rarely gummas and endarteritis and hemiplegia due to vascular syphilis Occasionally syphilis of the spinal cord produces the so-called combined tabes which consists of the symptoms of tabes plus pyramidal tract signs Vascular syphilis affecting the nervous system comes on earlier than other forms of neurosyphilis In vascular neurosyphilis *the spinal fluid may be and often is*, negative The diagnosis of paresis should never be made in an untreated patient if the spinal fluid and blood are negative Treatment of these *other forms of neurosyphilis* usually consists of penicillin and fever therapy

## THE SPINAL CORD

### COMPRESSION OF THE SPINAL CORD

The cord may be compressed by disease of the vertebræ such as tuberculosis and malignancy, by fractures and dislocations of the spine by tumors either within or without the cord by abscesses by erosion of the vertebræ due to an aneurysm by inflammatory reactions by Hodgkin s disease and by leukemia In view of the fact that practically all of the conducting pathways between the brain and the parts below are in the spinal cord definite changes in motion and in the control of the sphincters result Segmental or radicular motor and sensory manifestations will often help in locating the site of the lesion

### TUMORS OF THE SPINAL CORD

Tumors of the cord may be intramedullary or extramedullary and the latter type may be either subdural or extradural Intramedullary tumors are usually gliomas The ordinary subdural tumor grows from the pia and the arachnoid the spinal root or the dura The extradural tumor grows between the vertebræ and the dura While all varieties of neoplasms occur in or about the spinal cord the commonest spinal cord tumors are endotheliomas and fibromas They are usually benign and encapsulated An extramedullary tumor, occurring intradurally is the usual finding The size of the tumor varies greatly The tumor frequently makes a nest for itself in the cord It displaces the cord and signs of compression are practically always seen

Tumors are more common in the dorsal and lower cervical cord than elsewhere The *symptoms* usually are slow in onset and as a rule sudden paralysis does not occur Unless the neoplasm is growing from the anterior and antero lateral surface which is not common the earliest symptom is pain Most tumors originate from the lateral or postero-lateral aspects of the cord and involve a *posterior root early in the history* The pain is usually unilateral and, as the tumor enlarges may be bilateral It follows a root zone and if it occurs about the trunk or abdomen *it may be interpreted as a* unilateral girdle sensation The pain is increased by sneezing jarring or coughing and is of a sharp stabbing nature Intramedullary tumors do not give rise to radicular pain but may produce central pain Occasionally tenderness to percussion and rigidity of the spine occur at the site of the tumor The symptoms and physical signs will vary greatly depending upon the location of the lesion The common type of tumor growing from the postero-lateral as-

be a distinct loss of sensation in the distribution of the reflexes

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osteosarcoma may arise in the vertebral column from a neighborhood primary growth

The tumor usually involves two or more vertebræ In fact, in carcinoma all of the vertebræ may be diseased The roots are infiltrated as they pass to and from the cord The meninges are involved An important point to appreciate is that after a primary growth has been successfully removed metastasis to the spine may occur Acute angulation of the spine does not as a rule, occur and the exquisite tenderness seen in cases of Pott s disease is not common Pain is the most frequent and most distressing feature of this disease At first it is of a root nature the location of which depends upon the vertebra first affected As the disease progresses the patient develops usually suddenly symptoms of spinal cord compression The roentgenogram will aid greatly in the diagnosis but it is true here, as in Pott's disease that roentgen ray pictures made of the spine early in the disease may fail to show metastasis

Myeloma leukemia and Hodgkin's disease may involve the spinal cord directly or through metastasis to the vertebræ

*Treatment* of malignancy of the vertebræ is ineffectual The patient should be kept under the influence of narcotics or a cordotomy or lobotomy should be done Deep roentgen ray therapy or radium may be tried but are usually of no value except to relieve pain Testosterone and estrogens have been used for the relief of pain (*See* Chapter 28 )

## EPIDURAL AND SUBDURAL ABSCESS OF THE SPINAL CORD

Occasionally in the course of abscess formation anywhere in the body but more frequently secondary to boils on the back or on the neck a collection of pus or inflammatory material may localize in the epidural or more rarely in the sub dural space This usually occurs in the mid dorsal region The most constant early symptom is severe backache followed by root pains and then more or less slowly progressing pressure on the spinal cord with signs of block Fever leu kocytosis and other signs of infection are usually present There may be localized tenderness over the spine If the nature of the illness is recog nized operation should be done immediately with a fair chance of success

## CIRCUMSCRIBED SEROUS SPINAL MENINGITIS

This condition, which is usually confused with spinal cord tumor, is a circumscribed collection of fluid in the meninges The symptoms are indefinite and are usually those due to com pression of the cord which if long continued may lead to secondary degeneration It may come on as the result of meningitis but often the etiology is obscure Trauma may be a contributing factor Backache root pain weakness in the lower extremities and symptoms of a mild compression usually complete the picture The treatment is surgical evacuation of the fluid

## TUBERCULOUS SPONDYLITIS (CARIES OF THE SPINE POTT S DISEASE)

Tuberculosis of the spine usually begins in the bodies of the vertebræ occasionally in the joints or the ligaments and very rarely in the arches and processes The disease progresses rather slowly to caseation and necrosis The cord is not usually involved by deformity of the vertebræ or by the bone disease but by an extradural collection of the tuberculous pus The dura becomes greatly thickened but is rarely ruptured It is also unusual for a tuberculoma to be seen in the spinal cord of a patient suffering from Pott s disease As the vertebræ become more diseased a knuckling occurs at the site of the lesion The abscess which results from the tuberculous caries may point in the retropharyngeal space in the region of the psoas muscle or posteriorly While tuber culous caries may be primary it is practically always secondary to tuberculosis elsewhere in the body It occurs most frequently in the dorsal region and while most common in children it is frequently seen in adults At the site of compression the cord may be swollen but is usually compressed In a case of long standing secondary degeneration occurs in the cord

The first *symptom* is localized pain in the diseased vertebra Pain which is usually of a dull type is increased by any movement but especially by jarring sneezing or cough ing Early in the course of the disease the spine is held rigid by reflex action Tenderness on percussion will be found or, if the head is sharply depressed pain will

pect of the cord will produce pain of a radicular type, followed by hyperesthesia or loss of sensation in the distribution of the root or roots which are affected. If the tumor is far enough anterior to involve the anterior horns, signs of *compression of these structures* will be noted at the level of the tumor. As the tumor presses against the cord a Brown-Sequard paralysis which may not be entirely complete occurs. Bilateral pyramidal tract symptoms may be seen, and later on signs of interruption of all the pathways in the spinal cord may come on. If the tumor lies directly over the posterior columns, the *functions of the posterior columns and of the pyramidal tracts are severely interfered with.* If the tumor lies on the anterior aspect of the cord a syringomyelic loss of sensation may occur below the level of the tumor. Difficulty in the control of the sphincters appears as the spinal cord compression progresses. Reflexes of defense are seen in cases that have severe or complete paralysis. Signs of a subarachnoid block, most important in the diagnosis of a spinal cord tumor are present. *The cells in the spinal fluid are* not usually increased. The colloidal gold curve may show alterations. The roentgenogram, pantopaque and air myelography may be used as an aid in localization.

*Intramedullary tumors* are usually without pain except, and that rarely, of a burning type. *The symptoms are likely to be bilateral* and symmetrical and very often of a syringomyelic type. Before any suspected spinal cord tumor is operated upon, malignancy throughout the body should be ruled out, careful roentgen ray studies made of the spine, search made for syphilis both by clinical and laboratory *examinations and* the possibility of localized subdural infections ruled out.

The differential *diagnosis* is to be made from diseases of the vertebrae, various conditions which produce degeneration in the spinal cord such as syphilis, multiple sclerosis, the combined sclerosis of anemia, pachymeningitis and subdural abscess.

The correct *localization* is the *sine qua non* for surgical success. A tumor involving the *cauda equina* will bring about signs and symptoms according to the roots affected. Pain is a common and distressing symptom. Paralysis when it occurs is of the flaccid type. Loss of control of the sphincters and impotence takes place. Pain and other forms of sensation are lost. *Tumors of the conus* (the four lowest segments of the cord, i.e., S, 3, 4, 5 and coccygeal, 1) resemble symptomatically those of the cauda, with *the following exceptions*: (1) *lesions of the conus usually produce symmetrical, of the cauda, non-symmetrical symptoms and signs*; (2) saddle anesthesia is more common in lesions of the conus; (3) sphincter involvement and loss of potency occur more often in lesions of the conus; (4) fibrillations occur in conus disease; (5) dissociated loss of sensation is seen in conus involvement, *and (6) paralysis of the lower extremities and alteration of the patellar reflexes do not* happen as long as the lesion is confined to the conus; those signs are common in lesions of the cauda equina.

*Cervical cord tumors* often produce rigidity of the neck, spinal hemiplegia and ultimately tetraplegia. With a cervical tumor severe pain, atrophy, loss of the deep reflexes, *Horner's syndrome or Klumpke's syndrome* may be found.

Localization of the tumor will be made upon (1) the area in which the early pain of root irritation occurred, (2) the sensory level and whether it is segmental or root, (3) the extent of the motor paralysis, (4) the *presence of localized atrophy*, (5) reflex alterations or inequality.

Careful repeated sensory examination with comparison of the results with sensory charts will help most in the localization.

The *treatment* is surgical.

## TUMORS OF THE SPINE

Any form of malignancy including myeloma may involve the vertebral column but carcinoma and sarcoma are the most common. Carcinoma of the spine is always metastatic in origin. *It most frequently arises from a primary lesion in the lung*, prostate, rectum or breast, although carcinoma anywhere in the body may metastasize to the spine. It may occur at any time in the history of carcinoma and in a number of cases *the primary growth had not been* discovered before death. Sarcoma and

occur at the diseased vertebræ Spinal deformity in the nature of a kyphosis may occur at any time in the disease although, unless the vertebræ collapse kyphosis is a late symptom When the roots are affected sharp, shooting radicular pains of a type seen in any condition affecting a posterior root occur These pains may be unilateral or bilateral and, if sensation is tested in these painful areas, some loss of sensation will be found especially for pain The site of the radicular pains will naturally depend upon the level of the lesion The girdle sensation may occur at the site of the lesion Involvement of the anterior roots will cause atrophy flaccid palsy and a loss of the deep reflexes in their distribution As the cord is pressed upon by the cold abscess signs of a spastic paralysis occur below the level of the lesion Sensory symptoms also come on and if the disease is unchecked all forms of sensation and of motion are lost below the lesion Due to the involvement of the antero lateral tracts a loss of pain heat and cold may be the first sensory lack Sphincter disturbance trophic and vasomotor signs bed sores and urinary infections are seen The onset is usually slow taking weeks or months to develop but occasionally if the vertebra suddenly gives way or if the blood supply is interfered with by compression the signs may be acute in their manifestation If the lumbo-sacral region is the site of caries a flaccid palsy occurs in the lower extremities with excruciating pain If the cervical spine is involved flaccid paralysis in the upper extremities and a spastic paralysis below may be noted If a high cervical Pott's disease is present all four extremities may be very weak and spastic and respiratory disturbances and bulbar symptoms may also be manifested as the upper vertebræ are diseased Reflexes of defense and involuntary jerkings of the lower extremities are common physical signs when the cord is markedly compressed These signs practically always indicate severe involvement Fever is present or absent depending on the presence of complications or of tuberculosis elsewhere in the body About one-half of the patients die Those with involvement of the dorsal vertebræ have the best chance of a good outcome While the paralysis may clear up some people suffer permanent loss of power even though the tuberculous process heals The hunchback usually represents a healed Pott's disease

The spinal fluid is frequently xanthochromic and may coagulate spontaneously Signs of a subarachnoid block are usually present Roentgenograms will usually be characteristic but are often negative for evidence of the disease in its early stages It is imperative, therefore not to permit one negative roentgenogram to keep one permanently away from the diagnosis of Pott's disease Malignancy of the spine tumors of the cord, spondylitis spinal syphilis aneurysm and hysteria are to be considered in the diagnosis If every patient showing paralysis of spinal origin were subjected to careful roentgen ray studies of the spine spinal puncture for evidence of syphilis and block and careful repeated neurologic examinations only a rare case would be diagnostic problem

The *treatment* of this condition is primarily that of tuberculosis Orthopedic operations are sometimes indicated and some brilliant results come from them Extension and immobilization of the spine are necessary Streptomycin and other antibiotics should be given An air bed or water bed careful nursing, especially for the prevention of bed sores are important The evacuation of an abscess is indicated if present Even after paralysis has lasted some months complete recovery may occur

## INJURIES TO THE SPINAL CORD

The spinal cord may be injured by fracture dislocation fracture dislocation stab wounds bullet wounds concussion or by hemorrhage into the cord as a result of trauma the vertebræ escaping damage

As in skull fracture and cerebral implication injury is of importance in direct relation to the amount of cord damage done The cord may be completely severed or merely concussed Hemorrhage may occur into the substance of the cord The symptoms which come on as a result of fracture or fracture-dislocation gunshot wounds and stab wounds will vary with the location of the injury If the lesion is high bulbar

symptoms may be seen Root pains and the signs of a spinal cord compression which may vary from slight involvement to complete loss of all functions below the level of the injury may be seen Occasionally a Brown-Sequard syndrome may make up the picture Reflexes of defense may be detected If the cord is completely destroyed at a certain level a flaccid palsy with loss of all reflexes below may be seen (Bastian s law) If a patient with a complete lesion of the cord does not die from shock or injury within the first week or two, the lower end of the cord regains a certain amount of automatic function, including that of the bladder The reflexes may become extremely active below the lesion and the slightest stimulation below it may produce a series of mass reflexes, occasionally with evacuation of the bladder

## HERNIATION OR PROTRUSION OF INTERVERTEBRAL DISKS

Herniation or protrusion of an intervertebral disk has come to be recognized as a not uncommon cause of nerve root or spinal cord compression

*Etiology* —Since the majority of protruded disks are found in those regions of the spine where the vertebral column is subject to the greatest mechanical stress on heavy lifting or pushing it is thought that in most cases the protrusion results from trauma In many cases however no definite history of injury can be elicited It is possible that repeated strain or mild trauma incidental to the wear and tear of daily activity may result in degenerative changes in the disk, and that this is a contributing etiologic factor

*Pathology* —The most common site of the protrusion is found in the lower lumbar spine In over 90 per cent of cases the site of the lesion is at the third fourth or fifth lumbar vertebræ but protrusions also occur in the lower cervical and mid and low thoracic area The protrusion may be of a single disk or multiple Frequently there is an associated hypertrophy of the ligamentum flavum which extends between the laminæ and in some cases hypertrophy of this ligament alone is found to be the cause of symptoms

*Symptoms* —The condition is more common in men than in women The symptomatology varies somewhat depending on the region involved, but the most common complaint is back or neck pain, almost always intermittent in character, which is aggravated by coughing sneezing, or straining In some cases, a history may be obtained of the onset of the pain immediately following heavy lifting or straining This pain may later spontaneously subside only to recur some time later following subsequent trauma often of a mild character

In the cervical and thoracic regions, the symptoms and signs are more or less characteristic of an extramedullary cord tumor except that the pain is more likely to be intermittent In lateral herniations in the cervical area the pain often of a root character is referred to the neck or the upper extremity and weakness, sensory and reflex changes may be found in one arm or the other If the herniation however occurs in the midline symptoms referable to the neck and upper extremity may be minimal The outstanding symptoms are usually spasticity of the lower extremities and disturbances in gait Signs of pyramidal tract involvement are present but sensory signs and sphincter disturbances are minimal Such cases may simulate multiple sclerosis When the lumbar region is involved the patient complains of intermittent low back pain with or without radiation down the posterior aspect of one or both legs (sciatic nerve distribution) Frequently there is an accompanying spasm of the lumbar back muscles and a loss of the normal lumbar lordosis Tenderness may be present over the course of the sciatic nerve and Laseque s sign is usually positive The ankle jerk may be diminished or absent and much more rarely the knee jerk Radicular zones of hypesthesia and hypalgesia are found in about one third of the cases Muscular weakness may be present Sphincter disturbances are uncommon

Lumbar puncture may show the presence of some degree of block on jugular compression in about one half of the cases in which the herniation occurs in the cervical or thoracic region but when lumbar region is involved a block is seldom present and

occur at the diseased vertebræ. Spinal deformity in the nature of a kyphosis may occur at any time in the disease although unless the vertebræ collapse, kyphosis is a late symptom. When the roots are affected sharp shooting radicular pains of a type seen in any condition affecting a posterior root occur. These pains may be unilateral or bilateral and, if sensation is tested in these painful areas some loss of sensation will be found especially for pain. The site of the radicular pains will naturally depend upon the level of the lesion. The girdle sensation may occur at the site of the lesion. Involvement of the anterior roots will cause atrophy flaccid palsy and a loss of the deep reflexes in their distribution. As the cord is pressed upon by the cold abscess signs of a spastic paralysis occur below the level of the lesion. Sensory symptoms also come on and if the disease is unchecked all forms of sensation and of motion are lost below the lesion. Due to the involvement of the antero-lateral tracts a loss of pain heat and cold may be the first sensory lack. Sphincter disturbance trophic and vasomotor signs bed sores and urinary infections are seen. The onset is usually slow, taking weeks or months to develop but occasionally if the vertebra suddenly gives way or if the blood supply is interfered with by compression the signs may be acute in their manifestation. If the lumbo-sacral region is the site of caries a flaccid palsy occurs in the lower extremities with excruciating pain. If the cervical spine is involved flaccid paralysis in the upper extremities and a spastic paralysis below may be noted. If a high cervical Pott s disease is present, all four extremities may be very weak and spastic and respiratory disturbances and bulbar symptoms may also be manifested as the upper vertebræ are diseased. Reflexes of defense and involuntary jerkings of the lower extremities are common physical signs when the cord is markedly compressed. These signs practically always indicate severe involvement. Fever is present or absent depending on the presence of complications or of tuberculosis elsewhere in the body. About one-half of the patients die. Those with involvement of the dorsal vertebræ have the best chance of a good outcome. While the paralysis may clear up some people suffer permanent loss of power even though the tuberculous process heals. The hunchback usually represents a healed Pott s disease.

The spinal fluid is frequently xanthochromic and may coagulate spontaneously. Signs of a subarachnoid block are usually present. Roentgenograms will usually be characteristic but are often negative for evidence of the disease in its early stages. It is imperative therefore not to permit one negative roentgenogram to keep one permanently away from the diagnosis of Pott s disease. Malignancy of the spine tumors of the cord spondylitis spinal syphilis aneurysm and hysteria are to be considered in the diagnosis. If every patient showing paralysis of spinal origin were subjected to careful roentgen ray studies of the spine spinal puncture for evidence of syphilis and block and careful repeated neurologic examinations only a rare case would be diagnostic problem.

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The spinal cord may be injured by fracture dislocation fracture dislocation stab wounds bullet wounds concussion or by hemorrhage into the cord as a result of trauma the vertebræ escaping damage.

As in skull fracture and cerebral implication injury is of importance in direct relation to the amount of cord damage done. The cord may be completely severed or merely concussed. Hemorrhage may occur into the substance of the cord. The symptoms which come on as a result of fracture or fracture-dislocation gunshot wounds and stab wounds will vary with the location of the injury. If the lesion is high bulbar

The pyramidal tracts the anterior horn cells of the cord and sometimes the nuclei of the seventh, ninth, tenth and twelfth cranial nerves are affected The usual case begins with involvement of the anterior horn cells and the pyramidal tracts in the lower cervical and upper dorsal cord The cause of the disease is unknown Occasionally a patient who has had acute anterior poliomyelitis may later develop amyotrophic lateral sclerosis It is of interest that many sufferers with this disease give a history of having been unusually active in athletics or in occupations involving heavy use of the muscles for many years Trauma as a cause has to be considered but there is no definite evidence on which to base it A few cases have been reported in which the disorder developed in the upper extremities of workers using compressed air drills

*Symptoms* — The age of onset is usually between thirty and fifty years although the disease may occasionally be seen in childhood

The motor fibers are involved in the pons peduncles and occasionally even the cells of the motor cortex are affected The signs of the anterior horn disease are usually the first symptoms to occur and these are exhibited in the hands with a gradual progression upward so that the forearms arms shoulder girdles and neck muscles may become atrophic At the same time or shortly afterward pyramidal tract signs appear in the lower extremities the reflexes may also be increased in the upper extremities as long as there are cells remaining in the anterior horns to transmit the reflexes Claw hand results and the patient may ultimately be paralyzed in all four extremities When the cranial nerve nuclei are affected by the disease the signs of bulbar palsy ensue Pain is uncommon but a tired sensation may be noted in the muscles undergoing or about to undergo atrophy

The *prognosis* is poor most cases succumbing within three years although a few cases survive for longer periods The onset of a bulbar palsy always hastens the end which may be due in such cases to choking secondary to the lodging of a piece of food in the trachea or to an aspiration pneumonia

The *differential diagnosis* is to be made from spinal syphilis which may simulate very closely amyotrophic sclerosis progressive spinal muscular atrophy atrophy produced by arthritis syringomyelia and cervical Pott's disease

The *treatment* is usually ineffectual Wechsler reported improvement in some cases following the administration of vitamin E (alpha tocopherol) (ephynal) but this has not been confirmed Careful nursing selection of food which can be easily swallowed and the avoidance of overexertion are important

## PROGRESSIVE SPINAL MUSCULAR ATROPHY

This disease is rare only 10 cases having been seen at the Philadelphia General Hospital in a ten year period No verified cases were found in *a series of over 6000 neurologic autopsies* It begins in middle life although there is a familial form which may be seen in infancy or childhood The anterior horn cells of the spinal cord are involved and just as in amyotrophic lateral sclerosis the nuclei of the seventh ninth and twelfth cranial nerves may be affected The process which begins insidiously is slowly progressive affects the lower cervical and upper dorsal cord first from which it spreads both upward and downward

The *symptoms* are those of anterior horn disease Whereas amyotrophic sclerosis usually kills in less than three years sufferers from progressive spinal muscular atrophy may live five to twenty years

The *treatment* is essentially that of amyotrophic lateral sclerosis

## COMBINED SCLEROSIS DUE TO PERNICIOUS ANEMIA (POSTEROLATERAL SCLEROSIS)

The cord changes which occur in primary anemia commence in the posterior columns and in the pyramidal tracts both are involved at approximately the same time although disease of either one may slightly antedate the other Severe secondary anemia and occasionally cachexia from any cause may produce a similar picture Posterolateral sclerosis may also occur without any evidence of disturbance of the hematopoietic functions While the exact cause of the degeneration of the spinal cord is not known it is likely that the same *etiologic factor*

the only abnormality found may be an increase of the spinal fluid protein

*Diagnosis* —The diagnosis may frequently be established on clinical evidence alone (when the lumbar area is involved) on the basis of a history of intermittent low back pain aggravated by coughing straining or sneezing with pain radiating down one or both legs, but myelography is usually necessary particulary in cases of cervical herniation

*Treatment* —When the herniation is in the lumbar area conservative treatment including complete bed rest physiotherapy and administration of salicylates, will often give relief It should be tried for at least a month If the pain still persists or the patient has occurrent attacks surgical intervention is indicated While some cases are therby completely relieved of pain we have seen many patients in whom a protruded disk was found and removed at operation but who continued to have pain Surgery in cases with cervical herniation is dangerous but a decompressive laminectomy is often helpful

## HEMATOMYELIA

*Hemorrhage into the spinal cord* is practically always the result of trauma It usually involves the gray matter and most often that about the central canal It is important to appreciate that hematomyelia may occur without injury to the vertebræ One or more segments may be involved by the hemorrhage the location of which depends upon the site of the injury although the cervical and lumbosacral regions seem most susceptible to trauma While the trauma which causes it is usually direct cervical hematomyelia may follow a blow on the head Hematomyelia may also be caused by a fall on the buttocks or by landing on the feet after a fall of considerable distance

The *symptoms* are usually sudden in onset and are rarely delayed more than a few hours The extent of the paralysis will depend on the site of the hemorrhage At the level of the lesion there is loss of pain heat and cold and, if the hemorrhage has extended into the anterior horn cells signs of involvement of those parts Pyramidal tract signs usually occur below the level of the lesion, due either to the extension of the hemorrhage or to edema of the cord Sphincter disturbances occur at this stage and trophic and vasomotor signs may also be seen Signs of a complete transverse lesion may exist

Sudden death may occur if the lesion is a high one Some patients may recover completely, but some of them show residual conditions which are found at the point of greatest involvement of the spinal cord The symptoms due to edema of the cord clear up, but those due to hemorrhage are slow in disappearing and some of the symptoms may persist Syringomyelia may develop in a person who has been the victim of hematomyelia

The *diagnosis* in hematomyelia is made by the history of injury the absence of vertebral injury and the signs and symptoms enumerated above

The *treatment* of injuries to the cord should be conservative If the spinal cord has been injured by fracture or a fracture dislocation it is unlikely that the surgical intervention will bring about the recovery of the individual unless there is a spinal block proved by roentgen ray to be due to bony compression and not relieved by manipulative measures Operation in the stage of shock is absolutely contraindicated it certainly hastens the death of a number of these patients Competent nursing a sponge rubber mattress bed the use of an indwelling catheter with tidal drainage and careful regulation of the gastro intestinal tract are important things in the care of these patients Fresh air and sunshine the prevention of deformity passive movements especially to the large joints light general massage and extreme care of the skin will aid greatly the chances of recovery Attention should also be directed toward maintaining a normal blood protein level and providing an adequate vitamin intake

## AMYOTROPHIC LATERAL SCLEROSIS

Amyotrophic lateral sclerosis is a relatively rare disease involving the motor system

massage, orthopedic correction of any contractures or deformities and plenty of fresh air and sunshine are adjuncts in the treatment of this condition

## SYRINGOMYELIA

The term signifies an abnormal cavity in the spinal cord which is usually due to a congenital anomaly affecting the central canal Spinal gliosis produces the picture of syringomyelia because cavities are produced by the new growth especially in the central part of the cord Hematomyelia and hypertrophic cervical pachymeningitis may also lead to cavitation within the cord and produce symptoms somewhat similar to those of syringomyelia The level of the cord usually affected first is the lower cervical and upper dorsal

*Symptoms* — The early symptoms of syringomyelia are usually referable to the hands and consist of a loss of pain, heat and cold sensations and atrophy Due to a loss of pain sensation the patient frequently burns himself without experiencing discomfort and may have pathologic fractures without pain If the cavity spreads longitudinally the loss of sensation in the upper extremities becomes greater and will ultimately involve them entirely and later implicate part of the trunk If the descending root of the fifth nerve is implicated the loss of pain heat and cold may occur in the face Trophic disorders such as arthropathies painless felons pathologic fractures and bone necrosis, spontaneous amputation of the tips of the fingers and thickening of the fingers are seen Hemiatrophy of the face rarely occurs and is most likely due to sympathetic involvement Scoliosis and kyphoscoliosis in the cervical and dorsal regions are usually found If the cavity spreads high enough to involve the bulb signs of bulbar palsy due to syringobulbia may exist If it spreads transversely the pyramidal tracts are implicated and signs of this involvement are found below the level of the lesion The disease may be associated with other congenital deformities

The *differential diagnosis* should not be difficult if one remembers that a dissociated loss of sensation for pain heat and cold with preservation of touch and proprioceptive sensation is found at the level of the cavity along with anterior horn symptoms in the upper extremities and pyramidal tract symptoms in the lower extremities *The prognosis for cure is bad, but for life is good*, some cases continuing from twenty-five to fifty years

There is no drug which has any merit in the *treatment* of syringomyelia Radium and roentgen ray have been used with slight success Operative treatment for this has been recommended The cord is exposed and an opening made into the cavity (myelotomy) In our experience, the results of *operation are very unsatisfactory*

## MYELITIS

The spinal cord may be the seat of inflammation secondary to certain infectious diseases or may be a primary site of infection This condition is known as myelitis In degenerative and other noninfectious conditions the term myelopathy should be *more properly applied* Probably the commonest cause of myelitis is syphilis Trauma is not a cause of myelitis except in so far as it produces hemorrhage into the cord (*v* hematomyelia)

*Pathology* —When an entire section of the cord is involved it is referred to as transverse myelitis The inflammatory areas may be present in patches and be of a diffuse nature or they may be limited to one side of the cord and produce a Brown-Sequard paralysis The cord in myelitis on gross examination is softened and shrunken The spinal cord removed from rapidly fatal cases is of almost a putty consistency The vessels are the seat of round cell infiltration The ganglion cells are distorted and swollen as are also the myelin sheaths and the axis cylinders Fatty degeneration ensues and there is an accumulation of glia cells Microscopic examination shows descending and ascending degeneration of a secondary nature The meninges are frequently considerably involved especially in the syphilitic type

*Symptoms* —These will vary according to the location of the lesion and its severity During or shortly after an acute infection the

which produces *pernicious anemia* is responsible It is unlikely that the anemia itself causes the cord changes, because of *the fact that one occasionally sees combined* sclerosis before any change whatsoever has occurred in the blood The cord *implication* may take place during a remission of the blood picture As the disease progresses the entire white matter of the cord may be involved The disease used to be much more frequent than multiple sclerosis amyotropic lateral sclerosis, syringomyelia and chronic progressive spinal muscular atrophy, but now is infrequently seen probably due to the frequent nonspecific use of liver extract in general medicine and also to the improved quality of food eaten

*Symptoms* —The symptomatology varies somewhat, according to the parts of the cord diseased In the usual run of cases the following is the order in which the symptoms occur Paresthesias in the fingers and toes are an extremely common early symptom although the paresthesias may be limited either to the hands or the feet While pain is uncommon the involuntary jerking of the lower extremities which frequently occurs may produce pain by the overaction of the muscles The gait becomes involved and is of the ataxic type with an element of spasticity in it The involvement of the pyramidal tracts produces a spastic weakness below the level of the lesion with the ordinary signs of such disease If the sclerotic patches in the posterior columns are pronounced and occur at the level of the reflex arc, that particular reflex may be abolished even though the voluntary motor system be affected Sphincter disturbances and a girdle sensation may occur but if they do it is usually late in the course of the disease The results of physical examination of the nervous system *in the typical* case not far advanced will show pyramidal tract signs loss of the forms of sensation carried upward by the long fibers in the posterior columns *i e* sense of position of vibration and of tactile discrimination This may occasionally occur in other conditions, but is very characteristic of the combined sclerosis of pernicious anemia If the cervical cord is involved ataxia in the finger to-nose test, astereognosis and the other posterior column symptoms may be seen in the upper extremities Signs of peripheral nerve involvement are found in 25 to 40 per cent of the cases Pupillary disturbances and ocular palsies practically never occur The optic nerves are not usually affected, although rarely optic neuritis may be seen in pernicious anemia

Mental symptoms not uncommonly appear the patients are often garrulous, disorientated their memory fails and depression and delusions may be seen It is important to know that the mental symptoms and the spinal cord changes may occur before the anemia or during a remission The patient should be examined thoroughly from a general medical standpoint for the signs and symptoms of pernicious anemia if he presents on neurologic examination pyramidal tract and posterior column signs Before the advent of vitamin $B_{12}$ therapy the outlook was usually bad and the patient lived not more than three years Now the expectation of life is much greater and some of the nervous symptoms may be brought under control and the patient s life accordingly prolonged and physical signs of cord involvement actually disappear if treatment is begun early

The *differential diagnosis* is to be made from tabes peripheral neuritis posterolateral sclerosis of syphilis pellagra multiple sclerosis and tumor of the cord The singling out of the posterior and *lateral columns* without producing pain pupillary and ocular disturbances the negative tests for syphilis the absence of a spinal block *and the presence* of achlorhydria and a megaloblastic anemia should lead the diagnostician to a *correct conclusion*

The *treatment* is that of pernicious anemia but the action must be vigorous and prompt Liver and/or vitamin $B_{12}$ are indicated Folic acid is of no value because cord changes may become aggravated although the anemia improves It must be emphasized to the patient that treatment must be continued indefinitely otherwise relapse will occur Careful nursing the prevention of bed sores by cleanliness the use of an air bed or water bed and the prevention of infection of the genito-urinary system are important points to be considered Light

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not known but at the Philadelphia General Hospital the commonest conditions found at autopsy were syphilis and tuberculosis

The earliest *symptom* is pain of a root nature, which occurs at the level of the lesion This is followed by compression of the anterior roots or disease of the anterior horn cells which produces atrophic paralysis at the level In view of the fact that the lower cervical cord is more frequently affected the foregoing symptoms are first seen in the upper extremities especially the hands Horner's syndrome may occur from involvement of the eighth cervical and first dorsal roots As the condition progresses, the signs of compression of the cord occur with interruption of the functions of the sensory paths and of the pyramidal system Disturbance of the sphincters is also seen

If the process is syphilitic in origin other signs of neurosyphilis may be present Spinal tumor syringomyelia and caries of the spine will have to be differentiated

## FRIEDREICH'S ATAXIA

Family or hereditary ataxia is a rare chronic, progressive heredodegenerative disease of the nervous system beginning as a rule before the age of ten or twelve years It is more common in males and affects chiefly the posterior columns spino-cerebellar tracts and the pyramidal tracts and is associated at times with an atrophy or agenesis of the cerebellum The *symptoms* are ataxia loss of the deep reflexes although they may occasionally be exaggerated Babinski's sign dysarthria often of the scanning type nystagmus Club foot pes cavus Friedreich's toe which consists of extension of the first phalanx of the great toe with flexion of the second to a right angle, and scoliosis make up the physical deformities Occult spina bifida may also be seen If the disease is of long standing atrophy due to disease of the anterior horn cells may occur in the upper extremities The so-called Marie's hereditary cerebellar ataxia resembles Friedreich's ataxia in many ways except that it occurs after twenty or thirty years of age and is not so likely to be associated with skeletal defects

The greatest difficulty in *differential diagnosis* will be with juvenile tabes which will show the characteristic pupillary state and areflexia laboratory signs of syphilis and the absence of skeletal deformities although Charcot's joints and trophic ulcers may be seen Multiple sclerosis may be mistaken for Friedreich's ataxia although the former is very rare in childhood

*Treatment* of Friedreich's ataxia and Marie's hereditary cerebellar ataxia is unavailing Marriage of members of families in which Friedreich's disease is known to exist is ill advised but in cases of Marie's ataxia a familial history is rare

## DISEASE OF THE BLOOD VESSELS OF THE SPINAL CORD

Either of the arterial systems of the spinal cord posterior or anterior may be occluded as a result of the disease which is most frequently syphilis The free flow of blood through the vessels may also be interfered with because of tumors, either benign or malignant especially the latter It is also likely that the sudden paralysis which sometimes takes place in Pott's disease or carcinoma of the spine may be due to interference with the vascular system particularly the venous drainage The most outstanding symptoms therefore will be referable to the parts of the cord involved Sometimes however pyramidal tract signs are seen below the level of the lesion and there may be dissociated sensory loss (A Ornsteen) The arteries in the posterior aspect of the cord are more frequently involved than those of the anterior The usual cause is syphilis

## HERPES ZOSTER (ZONA OR SHINGLES)

Herpes zoster is an affection of the sensory spinal or cranial ganglia There are two types of herpes zoster one of primary viral origin which may even occur in epidemics the other due to secondary involvement of the ganglia by such conditions as syphilis tumor or perhaps by acute infectious disease It may be due to anything which can affect a sensory ganglion which is frequently the site of hemorrhage and destruction Secondary degeneration may occur both in the peripheral nerve and in the dorsal root

If the condition is due to an acute infection the *symptoms* may be of a general nature such as fever headache and malaise The first symptom is pain which is of a definite root nature and in the root distribution In many cases it is sharp and unbearable If the patient is examined at this stage it will be seen that there is hyperesthesia and perhaps a loss of pain sense in the distribution

patient may develop pain in his back often accompanied by a girdle sensation If the disease is localized to one or two segments pain, except at the level of the lesion, is not a common symptom but paresthesias frequently exist below the inflammatory reaction The involvement of the pyramidal tracts will produce the most alarming symptom as far as the patient is concerned and these signs usually run true to form Just as the deep reflexes are occasionally lost on the side paralyzed in apoplexy, so the deep reflexes may be lost in myelitis early in the history of the case, but they later usually become exaggerated The Babinski sign, ankle clonus and perhaps patellar clonus soon appear If the posterior columns are involved there will be a loss of sense of position, vibration and tactile discrimination, and disease of the anterolateral tracts will result in loss of pain heat and cold All reflexes at the level of the lesion will be abolished Disturbances of function of the sphincters are extremely common, the usual history is that there is first retention and then incontinence of urine Due to the difficulty in the control of the bladder infection of the urinary tract occurs frequently complicates the case and lessens the possibility of recovery While there may be incontinence of feces most cases have marked constipation Occasionally priapism is a symptom Trophic disorders, such as loss of sweat secretion rarely increase of sweat various vasomotor phenomena and bed sores, occurring especially over the heels and the sacrum are common symptoms Involuntary jerkings of the lower extremities with reflexes of defense (Sinkler s toe phenomenon) are frequently seen in severe forms and are sometimes mistaken for return of power The recovery of the patient depends in a large measure upon the prevention of bladder infection and bed sores Many patients do extremely well Others make no improvement and remain bedfast Extreme degrees of flexion may occur after the paralysis has existed for some months

Complete transverse lesions of the cord have followed the intrathecal injection of sulfanilamide penicillin streptomycin spinal anesthetics, and alcohol

The *diagnosis* is made by the history and a *more or less rapidly* occurring paralysis and loss of sensation below a definite level accompanied by paralysis of the sphincters Multiple sclerosis occasionally has a sudden onset sudden paralysis of the lower extremities may be the first symptom of that disease

The *treatment* is largely symptomatic The patient should be placed in bed and an air mattress or water mattress used Extreme care should be taken of the skin which should be bathed often with alcohol and powdered with a mild antiseptic Frequent change of position to prevent constant pressure on one particular point is imperative The fact that the patient is incontinent of urine makes the nursing job an extremely arduous one, inasmuch as the bed linen should be changed whenever it is soiled Catheterization should be postponed as long as possible Daily irrigation of the bladder with a mild antiseptic may be necessary The use of tidal drainage and urinary antiseptics especially sulfa drugs and antibiotics is probably the bladder treatment of choice A daily enema will usually be necessary and occasionally a laxative should be given The lower extremities should be protected with a cradle and a good position at the large joints maintained if necessary with splints Daily passive movements to the large joints is also indicated Hydrotherapy and physiotherapy are of service when the patient begins to recover and will serve to relieve the spasticity in the lower extremities The body nutrition should be maintained a high protein diet with supplemental vitamins should be given and the serum protein level checked from time to time

## HYPERTROPHIC CERVICAL PACHYMENINGITIS

As the name indicates this is a thickening of the membranes especially the dura which may readily be twelve times the normal thickness The thickening of the dura is intense and causes the meninges to adhere to each other as well as to the roots and the spinal cord The cord is compressed and later on may be the seat of a rim degeneration secondary degeneration and even cavitation While the lower part of the cervical cord is most frequently involved the process may extend to include the entire cord and even the medulla and pons The exact etiologic factor is

Epidemics usually occur during the summer and early fall months and the incidence drops off abruptly about the time of the first frost. Sporadic cases occur, however, throughout the year. The sexes are about equally involved. The great majority of cases are children but adults likewise are affected, possibly more so in recent years. When poliomyelitis occurs in pregnant women transmission to the fetus is very rare.

*Pathology.*—The anterior horn cells of the spinal cord, the nuclei of the motor cranial nerves, and the meninges are chiefly involved. Occasionally changes are noted in the motor cortex, white matter, basal ganglia and cerebellum. The characteristic pathologic change is that of hyperemia, edema and perivascular round-cell infiltration. The anterior horn cells, particularly those in the lumbar and cervical areas, are swollen, show chromatolysis and marked neuronophagia. In severe cases many of the anterior horn cells disappear and are replaced by glial cells and ultimately the motor nerve roots, nerves and muscles become atrophic. In addition to the changes in the nervous system hyperplasia of the lymphoid tissue throughout the body occurs.

*Symptoms.*—The clinical picture tends to be quite variable. Cases are usually classified as abortive, nonparalytic, paralytic and bulbar.

The abortive type is the most frequent. The illness may be so mild that it passes unrecognized. In other cases there is a sudden onset with a fever of 101 to 102, malaise, headache, sore throat, anorexia, constipation or occasionally diarrhea and vomiting. The neurologic examination is negative and the spinal fluid may show no alteration. The symptoms subside within 24 to 72 hours and the patient thereafter is well and without residua. In the absence of an epidemic such cases are often considered as merely acute upper respiratory or gastrointestinal infections and poliomyelitis is seldom considered. However, during epidemics it is possible that many cases described as being of the abortive type are not actually poliomyelitis.

About half the severe cases run a biphasic or dromedary febrile course. A brief mild nonspecific illness of short duration clinically closely akin to the abortive type is followed by apparent recovery. After four to seven days fever and headache along with signs of central nervous system involvement appear. In other and more typical cases the headache and fever continue. Occasionally one sees a patient with hyperesthesia who resents being disturbed. Pain in the trunk and limbs may be present along with localized muscle and nerve trunk tenderness. Slight muscle twitchings may be noted. Retraction of the head, nuchal and spinal rigidity and Kernig's sign are usually present. In some cases apathy, drowsiness and stupor occur. There may be retention of urine and rarely convulsions. In the nonparalytic cases the symptoms subside; in others the development of paralysis ushers in the paralytic phase.

While any part of the spinal cord may be involved in the ordinary type of the disease, the lumbo-sacral region is most frequently affected and usually in an irregular manner. The paralysis, which is a flaccid one, will depend upon the anterior horn segments involved and will be in the distribution of those segments. The muscles of the abdomen, the back and even those of the neck may be paralyzed. Certain writers believe that the commonest cause of scoliosis is poliomyelitis. An entire extremity or a part of it may be paralyzed and the involvement may be so irregular as to produce a paralysis of an upper and the opposite lower extremity.

The paralysis is accompanied by a loss of the deep and superficial reflexes in the segments involved, and after a week or two there may be loss of contractibility of the muscles to faradism and galvanism, and in severe cases complete reactions to degeneration. As a rule the height of the paralysis is reached within three to five days of the onset. In many cases, especially infants, the exact date of paralysis is not known. Some of the cases described under the heading of Landry's paralysis are in reality instances of poliomyelitis. Involvement of the bulb or of the ocular nuclei may occur either as distinct types of the disease or as part of the general picture. The virus of poliomyelitis can also affect the motor cortex, producing hemiplegia of the spastic type. To

of the root affected From a few hours to a few days after the onset of pain the skin throughout the entire course or a part of the course of the nerve becomes red and the site of vesicles The skin disturbance lasts a few days, although if infection occurs the skin lesions may not clear up for two or three weeks Scarring and pigmentation especially the latter, may appear and persist After the eruption has taken place pain may subside, but, on the other hand, the pain may persist This is especially so when the herpes involves the face or if it occurs in an elderly person While any part of the body may be affected herpes zoster most usually implicates the chest Geniculate ganglion herpes occurs in the ear and is usually accompanied by Bell s palsy The disease is practically always unilateral and recurrences are rare Corneal ulceration with secondary infection may occur in herpes of the ophthalmic division of the fifth nerve As an evidence of meningeal reaction lymphocytosis of the spinal fluid is seen Rarely paralysis due to implication of anterior roots with the usual signs of such involvement may develop The prognosis is good but intractable neuralgic pain may be an uncomfortable sequence

In considering the *treatment* it is important to find the cause for the condition The possibilities of spinal tumor, Pott s disease and neurosyphilis should be considered and eliminated Locally alcohol saturated with boric acid and frequently applied to the vesicles will cause them to dry up Aureomycin has been reported as being beneficial in relieving the pain in some cases Drugs such as acetylsalicylic acid acetphenetidin and perhaps even codeine or morphine may be necessary Obstetrical pituitrin 1 cc several times daily, thiamin frequent small pox vaccinations autohemotherapy and roentgen irradiation have also been recommended, but in some instances it may be necessary to do root block with novocaine or if this procedure fails to section the root involved

## ACUTE ANTERIOR POLIOMYELITIS

*Synonyms* —Infantile spinal paralysis Heine-Medin disease

*Definition* —Acute anterior poliomyelitis is an acute infectious disease of viral etiology with a predilection to involve the nervous system particularly the anterior horn cells and the nuclei of the motor cranial nerves It occurs endemically but more frequently as an epidemic disease especially during the summer months Although adults are not spared the disease more frequently occurs in children

*Etiology and Epidemiology* —The infectious agent in a filterable virus Much remains to be learned regarding the natural mode of transmission The virus probably enters the body by way of the upper gastrointestinal tract including the mouth and pharynx It has been isolated from the pharynx just prior to the onset and during the first few days of symptoms and from the stools four to six weeks or more after the onset Once the infectious agent has gained access to the body it spreads to the central nervous system probably by way of the lymphatics The incubation period is not exactly known but is probably about ten days to two weeks Healthy human carriers who harbor the virus but never show symptoms are frequently encountered during epidemics Dissemination of the disease may occur by direct contact through carriers or by contact with contaminated objects such as food and sewage During an epidemic the virus has been isolated from flies and it is possible that insects may be a vector it is also found in high concentrations in sewage from areas where the number of clinical cases is large The virus varies in infectivity Although multiple cases within the same family occur with fair frequency, usually only one member is infected and the incidence in nurses physicians and others who come into close contact with active cases is relatively rare There is some evidence to suggest that severe muscular exercise immediately prior to exposure to the infectious agent may contribute to the development of a severe form of the disease and robust children have no greater immunity than the markedly undernourished Bulbar types of the disease occur frequently in children whose tonsils have been removed during an epidemic

Epidemics usually occur during the summer and early fall months and the incidence drops off abruptly about the time of the first frost Sporadic cases occur however throughout the year The sexes are about equally involved The great majority of cases are children but adults likewise are affected possibly more so in recent years When poliomyelitis occurs in pregnant women transmission to the fetus is very rare

*Pathology* —The anterior horn cells of the spinal cord the nuclei of the motor cranial nerves and the meninges are chiefly involved Occasionally, changes are noted in the motor cortex white matter basal ganglia and cerebellum The characteristic pathologic change is that of hyperemia, edema and perivascular round-cell infiltration The anterior horn cells particularly those in the lumbar and cervical areas are swollen show chromatolysis and marked neuronophagia In severe cases many of the anterior horn cells disappear and are replaced by glial cells and ultimately the motor nerve roots nerves and muscles become atrophic In addition to the changes in the nervous system hyperplasia of the lymphoid tissue throughout the body occurs

*Symptoms* —The clinical picture tends to be quite variable Cases are usually classified as abortive nonparalytic paralytic and bulbar

The abortive type is the most frequent The illness may be so mild that it passes unrecognized In other cases there is a sudden onset with a fever of 101° to 102 malaise headache sore throat anorexia constipation or occasionally diarrhea and vomiting The neurologic examination is negative and the spinal fluid may show no alteration The symptoms subside within 24 to 72 hours and the patient thereafter is well and without residua In the absence of an epidemic such cases are often considered as merely acute upper respiratory or gastro intestinal infections and poliomyelitis is seldom considered However during epidemics it is possible that many cases described as being of the abortive type are not actually poliomyelitis

About half the severe cases run a biphasic or dromedary febrile course A brief mild nonspecific illness of short duration clinically closely akin to the abortive type, is followed by apparent recovery After four to seven days fever and headache along with signs of central nervous system involvement appear In other and more typical cases the headache and fever continue Occasionally one sees a patient with hyperesthesia who resents being disturbed Pain in the trunk and limbs may be present along with localized muscle and nerve trunk tenderness Slight muscle twitchings may be noted Retraction of the head nuchal and spinal rigidity and Kernig s sign are usually present In some cases, apathy drowsiness and stupor occur There may be retention of urine and rarely convulsions In the non paralytic cases the symptoms subside in others the development of paralysis ushers in the paralytic phase

While any part of the spinal cord may be involved in the ordinary type of the disease the lumbo-sacral region is most frequently affected and usually in an irregular manner The paralysis which is a flaccid one will depend upon the anterior horn segments involved and will be in the distribution of those segments The muscles of the abdomen the back and even those of the neck may be paralyzed Certain writers believe that the commonest cause of scoliosis is poliomyelitis An entire extremity or a part of it may be paralyzed and the involvement may be so irregular as to produce a paralysis of an upper and the opposite lower extremity

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this condition the term of polioencephalitis is applied The involvement of the cranial nerves will produce paralysis in the distribution of the nuclei affected Meningitic types in which Kernig's sign stiff neck and pain on manipulation of the paralyzed extremity predominate, are frequent Tenderness on percussion over the side of the pathologic process may be found Cerebellar symptoms due either to involvement of the cerebellum or of the cerbellar peduncles, may occasionally be encountered Those patients with involvement of the bulb not infrequently die suddenly Loss of sensation does not occur The bladder may be paralyzed Trophic lesions and bed sores are extremely uncommon complications, although the skin of the paralyzed extremity may be cool mottled and show disturbance of sweat secretion

*Bulbar Type* —In the bulbar type the most frequent nerves involved are the 7th 9th, 10th, 11th, and 12th The early signs therefore are inability to swallow collection of saliva in the posterior pharynx the speech has a nasal twang fluid regurgitates through the nose Facial paralysis of one or both sides may occur

In the acute and paralytic phases, the leukocytes in the blood are usually not increased a few cases may show leucocytosis The spinal fluid is usually not under increased pressure, is clear shows excessive total protein which is of diagnostic importance, and has a normal percentage of sugar A mild alteration of the colloidal-gold curve may be seen The cells are definitely increased from 10 to a few hundred Though polymorphonuclear leukocytes predominate in the early stage of the disease, they quickly give way to lymphocytes

Following the onset of paralysis and the subsidence of the signs of infection the muscle tenderness gradually disappears and the convalescent phase begins Those muscles whose anterior horn cells are permanently damaged will begin to atrophy and show the reaction of degeneration while other muscles may begin to show some signs of returning function In many cases the residual paralysis may be much less than would it first appear since many anterior horn cells are only temporarily disturbed and may recover function The duration of the convalescent phase varies with the individual case but improvement may continue for as long as eighteen months

The chronic stage represents the end result of the disease The affected muscles are atrophied, the deep reflexes are absent and muscle power is impaired Flaccid palsies or paralyses contractures, and deformities such as scoliosis, lordosis and talipes equinus may be noted along with various trophic changes The skin over the paralyzed muscles may be cold dry and cyanotic the paralyzed limb may show varying degrees of dysgenesis

*Diagnosis* —Once the disease is in full bloom but little diagnostic difficulty will be encountered In abortive pre paralytic and mild non paralytic stages the problem may be more difficult In times of an epidemic all illnesses characterized by fever headache gastrointestinal symptoms, sore neck or back and muscle tenderness should be regarded with suspicion as possible cases of poliomyelitis but other conditions should be also considered Pott s disease hip disease meningitis of any type encephalitis lymphocytic choriomeningitis acute infectious neuronitis and infantile scurvy are often mistaken for acute anterior poliomyelitis The so-called pink disease may also be wrongly diagnosed poliomyelitis Rheumatic fever may be mistaken for infantile paralysis Occasionally during epidemics of infantile paralysis instances of widespread involvement of the white matter of the cord may be seen and the picture of myelitis rather than poliomyelitis results

The spinal fluid findings may be helpful but are not essential to the diagnosis since the spinal fluid may be normal in abortive cases and may even remain normal in non paralytic and paralytic cases

*Prognosis* —The prognosis varies in different epidemics the mortality being from 5 to 25 per cent Extreme restlessness and apprehension sometimes connote a poor prognosis The most unfavorable cases are those with bulbar symptoms in which the mortality rate is usually greater than 50 per cent It is impossible to predict whether paralysis will occur in a given case or if it

does, how extensive will be the residual deformity It is certainly true that there are many cases of acute poliomyelitis which are extremely mild and never develop paralysis When paralysis has occurred, it may clear up rapidly or no improvement may occur However it is important to keep the flag flying and to be optimistic as to the amount of recovery possible As in any paralysis of the peripheral nerve or anterior horn type, the early return of normal reactions to galvanism or faradism is a good prognostic omen Less than 25 per cent of the patients with the paralytic form suffer severe permanent disability, about 25 per cent have mild disabilities while over half recover without residua The mortality rate varies from 1 to 10 per cent of the total number of cases

*Prevention* —Since the mode of spread of the disease is unknown no definite preventive precautions can be established However, during epidemics the following measures are advisable All known cases should be isolated usually for a three week period Contact with patients suffering from unexplained minor illnesses should be avoided Personal cleanliness should be carefully maintained particularly the hands should be washed before eating Elective tonsillectomies and tooth extractions should be avoided Fatigue and extreme overexertion should be guarded against Food should be protected from flies Swimming in water which may be contaminated by sewage is to be avoided

*Treatment* —There is no specific treatment for the disease and no drug or antibiotic at present available is of value Convalescent serum at one time was extensively used but experience has shown it to be without beneficial effect and given into the subarachnoid space may grossly aggravate the disease Plasma likewise is useless Until such a time as specific measures become available therapy must be symptomatic and supportive

Usually bed rest an adequate fluid intake and a light nutritious diet along with proper care of elimination are adequate in the management of patients with the abortive or mild non paralytic types The importance of rest is to be stressed since undue physical exertion in the early stages of the disease appears to precipitate paralysis In the more severe stages of the disease the patient should be made as comfortable as possible Mild sedatives and analgesics may be indicated An adequate fluid intake should be maintained and the bowels should be kept open by enemas or mild purgatives Urinary retention should be treated by the administration of prostigmine or other parasympathetic stimulants Boards under the bed and foot boards are of help in preventing undue deformities when paralysis develops Early splinting is to be avoided Hot packs may be helpful in relieving the pain and discomfort Curare and prostigmine are used in some clinics to relieve muscle spasm Personally we have not found them of value

The Kenny treatment has attracted far greater attention than it warrants Its only value lies in its stress on the advantages of early physiotherapy and the avoidance of too early splinting the latter treatment being advised by orthopedists and not by neurologists

Respiratroy failure due to either paralysis of the muscles of respiration or to involvement of the respiratory center in the medulla requires vigorous therpeutic measures In respiratory muscle paralysis the Drinker respirator may be lifesaving but it is of no value and may even be harmful when respiratory difficulties are due to bulbar involvement With respiratory embarrassment prophylactic penicillin to prevent pneumonia should be administered When respiratory failure is due to bulbar involvement continuous inhalation of a humidified mixture of 95 per cent $O_2$ and 5 per cent $CO_2$ is of value and the tracheal airway must be kept patent by the use of a suction apparatus and postural drainage Bulbar involvement may be treated by tracheotomy the insertion of a tracheal tube and the administration of continuous oxygen Again the airway must be kept free by suction The patient s fluid and nutritive requirements must not be forgotten Parenteral fluid should be given A liquid diet high in calories may be given by tube with due care being taken to prevent aspiration following regurgitation or vomiting

this condition the term of polioencephalitis is applied. The involvement of the *cranial* nerves will produce paralysis in the distribution of the nuclei affected. *Meningitic* types in which Kernig's sign, stiff neck and pain on manipulation of the *paralyzed* extremity predominate, are frequent. Tenderness on percussion over the *side of the* pathologic process may be *found*. Cerebellar symptoms, due either to involvement of the cerebellum or of the *cerbellar peduncles* may occasionally be encountered. Those patients with involvement of the bulb not infrequently die suddenly. Loss of sensation does not occur. The bladder may be paralyzed. Trophic lesions and bed sores are extremely uncommon complications although the skin of the paralyzed extremity may be *cool, mottled and* show disturbance of sweat secretion.

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The vision may be disturbed in *multiple* sclerosis long before changes of the fields or eye grounds However with prolonged observation pallor of the disks especially of a bitemporal nature, may be found Impairment of the fields particularly central scotomas for color is often present and may occur in the absence of changes in the disks Ocular palsies are not as prominent as pallor of the disks and nystagmus The abdominal reflexes due to involvement of the pyramidal tracts disappear The symptoms of pseudobulbar palsy especially the emotional disturbance *and a general euphoric trend may* be seen

A frank psychosis is occasionally seen in multiple sclerosis and while it may take on the picture of a depression it is more often characterized by euphoria excitement and delusions If the patient with multiple sclerosis lives long enough, he may present the picture of complete dementia The blood Wassermann *is negative the spinal fluid* as a rule, shows a normal cell count normal globulin content and a negative Wassermann The colloidal gold curve sometimes shows an alteration of the first zone type or the curve may be high in the middle The disease which is slightly more common in males at one time was considered to be rare but in recent years its occurrence has not been *uncommon*

Remissions are common in the disease especially in those cases which begin acutely A remission may last from a few months to years The duration of life is from one to twenty five years the average being about ten

Although some patients suffering from multiple sclerosis become chair- or bed ridden in a few years *there are many cases* which run a benign course

*Diagnosis* —The conditions which may be confused with multiple sclerosis are disseminated neurosyphilis arteriosclerosis the combined sclerosis seen in pernicious anemia Friedreich s ataxia tumors of the cerebellum and the cerebellopontile angle tumors of the cord hysteria multiple areas of softening or diseased areas as the result of trauma and pseudosclerosis While some of these conditions undoubtedly will cause confusion at times mistakes in diagnosis can be kept to a *minimum The signs symptoms and laboratory* findings of neurosyphilis the blood picture and the gastric analysis in pernicious anemia signs and symptoms of a tumor should keep the record clear as far as these conditions are concerned Because of a remission which may apparently be brought about by psychotherapy, along with an initial onset during a period of emotional stress the diagnosis of hysteria is frequently made A careful examination with the elicitation of signs such as nystagmus and Babinski s sign which are always due to an organic involvement of the central nervous system should avoid the wrong diagnosis In the so-called acute multiple sclerosis a differential diagnosis is extremely hard to make between that form of disease and disseminated encephalomyelitis The mere fact that acute involvement of the nervous system of an apparent inflammatory type clears up does not rule out the possibility *that the case may be one of multiple* sclerosis

*Treatment* —There is no specific therapy for the disease Fever therapy iodides histamine quinine heparin and Dicumarol have all been tried without result The patient should be placed in the best possible health foci of infection removed and freedom from work and worry instituted A *high vitamin B diet, and intramuscular* liver injections are worthy of a trial Massage hydrotherapy and reeducation to keep the muscles and skin in good condition should greatly aid the patient Later on as the patient becomes chair or bed ridden careful nursing is required and the attending physician should be tactfully encouraging and should use as much constructive *psychotherapy as possible*

## THE BRAIN

### FOCAL SIGNS DUE TO LOCALIZED CEREBRAL LESIONS

Lesions of the *frontal lobe* produce as a rule some changes in the intellectual capacity of the individual Irritability, loss of memory undue jocosity and disorientation in space and position along with a loss of drive or initiative may characterize

In paralytic cases in the convalescent phase, physiotherapy in the form of gentle massage passive and active motion and muscle re-education exercises are of value Splints and braces may be necessary and helpful and nonparalyzed muscles should be strengthened It should ever be remembered that there is an inherent tendency for the paralyzed muscles to regain a considerable degree of function and spontaneous improvement may be expected to occur up to 18 months to two years after the acute illness In some epidemics as high as 85 per cent of the cases with paralysis may eventually show a practically complete return of muscle function

In old cases, orthopedic procedures may be indicated Occupational therapy is helpful not only in strengthening weak muscles but also in aiding the patient to acquire skills which may be economically valuable and in building and maintaining morale

## MULTIPLE SCLEROSIS

*Synonyms* —Disseminated sclerosis Insular sclerosis

This is a chronic disease of the central nervous system, although it may run an acute or subacute course The cause of the disease is not known Experimentally demyelination has been produced as an allergic response and possibly allergy plays some role in the causation In a few instances the disease may be familial occurring in siblings or in both parents and children It may follow after an acute infectious disease Apparently in some cases it has been precipitated by pregnancy Trauma produces a condition which simulates multiple sclerosis

The age at onset is usually between twenty and forty years, although cases do occur earlier and later in life In cases occurring in childhood, especially in more than one member of a family, one is more likely to be dealing with a familial disease of the extrapyramidal system

*Pathologically* the disease is distinguished by numerous sclerotic patches scattered through the central nervous system These patches are characterized by a degeneration of the myelin sheaths and a preservation of the axis cylinders which, however, are affected later The optic nerves are involved, usually in the nature of a retrobulbar neuritis The irregularity and the number of the sclerotic patches frequently makes for peculiar and bizarre symptoms The white matter of the central nervous system is much more affected than the gray The pyramidal tracts, due to their great length are practically always involved by sclerotic patches

*Symptoms* —The onset of the disease, while usually insidious, may be abrupt Sudden blindness, hemiplegia, crural paraplegia and an ocular palsy may come on quickly and clear up The preservation of the axis cylinders accounts for the return of power The history in the ordinary case is usually first of numbness parasthesia and weakness in the lower extremities, followed by ataxia and tremor in the upper extremities ocular disturbance and involvement of speech The ocular signs are dimness of vision blindness nystagmus or perhaps a palsy of an ocular nerve The classical *triad of Charcot* namely tremor scanning speech and nystagmus was at one time considered the chief symptoms in multiple sclerosis but it occurs only as a late manifestation in about 25 per cent of cases One should be extremely hesistant in diagnosing multiple sclerosis without the presence of pyramidal tract signs While sensory disturbances may be present one would expect to see such changes more often than they occur signs of posterior column disturbance are most common The type of sensory loss will depend upon the exact location of the sclerotic patch responsible for it The tremor which is called an intention or action tremor is made worse by movement While it is usually best brought out in the finger to-nose test any voluntary action on the part of the patient may throw not only the particular part in action but also the entire body The disturbance of speech dysarthric in nature is probably produced in the same way as the tremor While it is sometimes of a scanning nature it may simulate the speech of general paresis Nystagmus which may be lateral vertical or rotary or all three is usually due to a patch of sclerosis in the medulla or pons

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visual fibers may be involved and temporal lobe symptoms also brought about

*Occipital Lobe* — The chief localizing symptom here produced is homonymous hemianopsia in the contralateral visual fields. Irritation of the visual cortex or of the optic radiations may produce visual hallucinations which are crude and often ill-defined.

Implication of the *optic thalamus* produces disturbance or loss of all forms of sensation on the opposite side of the body accompanied by dysesthetic phenomena. For example if a piece of ice or a very hot test tube is placed on the hand of the affected side the patient cannot appreciate them as cold or hot but says that it produces a nasty disagreeable painful sensation. Deep pressure and scratching with a pin will often produce the same unpleasant sensation. While not pathognomonic of lesions of the optic thalamus such symptoms are extremely suggestive. Spontaneous disagreeable and painful sensations may occur on the contralateral side. If the *pulvinar* is involved hemianopsia on the opposite side may occur. Mild lesions of the thalamus may not produce the devastating signs mentioned.

Lesions of the *corpus striatum* produce various types of involuntary movements and rigidity. If the internal capsule is not involved by lesions of the optic thalamus and corpus striatum pyramidal tract signs will not be present on the opposite side.

Involvement of the anterior part of the *internal capsule* produces hemiplegia on the contralateral side. Monoplegia is rarely if ever produced by a lesion in this locality. Implication of the posterior part of the internal capsule produces sensory loss and hemianopsia on the opposite side.

*Corpora Quadrigemina* — This locality contains functions which are chiefly visual and auditory. The superior corpora quadrigemina have to do with vision and the inferior with hearing. In lesions of this area the pupils are often dilated and fixed. Paralysis of upward gaze (Parinaud's syndrome) and signs of ocular palsies especially of the third nerve are common. Extension of the lesion to the red nucleus and superior cerebellar peduncles produces tremor and ataxia. Tumors of the quadrigeminal plate by compressing the aqueduct are prone to give rise to internal hydrocephalus with accompanying signs of increased intracranial pressure.

*Pineal Body* — Lesions of this structure which are usually tumors produce in effect the same symptoms as those of the corpora quadrigemina. In addition to the signs enumerated above pubertas precox may occur.

*Cerebral Peduncle* (*Crus Cerebri*) — A lesion of the anterior portion of this structure produces one of the typical forms of crossed hemiplegia namely third nerve paralysis on the side of the lesion and the face arm and leg on the opposite side. This is Weber's syndrome. If in addition the dorsal part of the peduncle is involved tremor and ataxia occur in the opposite limbs. The tremor simulates to some degree that of paralysis agitans but usually is not decreased on voluntary effort. The ataxia and tremor in such a case are due to implication of the red nucleus. This symptom complex is referred to as Benedikt's syndrome.

*Pons* — The type of crossed paralysis found in lesions of the pons is for the fifth sixth and seventh nerves to be paralyzed on the side of the lesion and the extremities on the opposite side. The common type of paralysis is for the seventh nerve on the ipsolateral side of the body to be involved and the extremities on the contralateral side. This is Millard Gubler type of crossed paralysis. The sixth nerve may be implicated in a Millard Gubler paralysis. Gliomas of the pons may assume great size before definite symptoms are produced. Tumors of the pons do not usually cause choked disk.

*Medulla* — Alternating hemiplegia and cranial nerve paralysis may occur from lesions of the medulla. Lesions implicating both pyramidal tracts will produce symptoms of such involvement below the level of the lesion. Occlusion of the posterior inferior cerebellar artery results in softening in the dorso-lateral portion of the medulla with involvement of the descending root of the fifth nerve and the spinothalamic tract which causes a crossed sensory paralysis of the face on the side of the lesion and extremities and trunk on the opposite. The patient tends to fall to the side of the lesion due to involvement of the restiform body

disease of the frontal lobe Weakness of the contralateral side of the face may be the only physical sign detected but it must be interpreted with care inasmuch as many normal persons cannot move both sides of the face equally well In blinking the eye on the affected side of the face may close just a *little later than its fellow* Lesions at the base of the frontal lobe, especially tumors, may cause diminution or loss of smell and may also, by pressure on an optic nerve, produce primary optic atrophy on the side of the lesion and choked disk on the opposite side (Kennedy syndrome) Lesions of the lower part of the third left prefrontal gyrus in a right handed person will cause motor aphasia The attention is often difficult to obtain and hold Inattention to the sphincters leads to frequent soiling of the person

Lesions, especially tumors of the *corpus callosum*, are characterized chiefly by various mental symptoms due to interference with the association tracts In some cases these are limited to apathy and indifference while in others there is difficulty in concentrating personality changes, or a frank psychosis Memory is defective, speech difficult or impossible and apraxia a common symptom The mental symptoms are often mistaken for senile dementia or paresis Patients frequently do not respond to questioning and look blankly at the examiner Paralysis or weakness of *the extremities may* occur, but usually mean extension of the lesion into the motor parts Cranial nerve symptoms are not present

The upper part of the *motor cortex* (paracentral lobule) governs movement of the lower part that is the toes and foot of the opposite side of the body The lowest part of the left motor cortex is in close relation to Broca's area The center for the lower extremity is supplied by a branch of the anterior cerebral artery and the rest of the motor cortex by a branch from the middle cerebral artery An occlusion of the artery supplying the foot and leg centers may produce a monoplegia on the opposite side with the usual signs of pyramidal tract disease Involvement of the motor cortex will produce weakness and finally paralysis of the opposite side of the body and if the lesion is an irritative one, Jacksonian epilepsy or partial continuous epilepsy may be present on the weakened side A slowly progressive hemiplegia is quite characteristic of a new growth, a slow hemorrhage or thrombosis or cerebral abscess Early in the stage of a gradually growing lesion *segmental cerebral monoplegia* may occur Sensory loss does not occur in a lesion which is pre Rolandic Subcortical lesions produce a progressive hemiplegia and in some cases focal epilepsy Irritation of the motor cortex instead of causing frank Jacksonian epilepsy may produce twitching movements on the opposite side

In a right handed individual lesions of the *right temporal lobe* which is in the present state of knowledge a silent area are difficult to recognize and it is only after neighboring structures are involved that localizing signs can be detected Lesions of left temporal lobe (first and second convolutions) cause a sensory aphasia or word deafness with a jargon speech Lesions deep in the temporal lobe may involve the optic radiation causing thereby defects in the visual fields of the opposite side These defects in the early stages are of a quadrantic nature Later on hemianopsia is produced

Lesions involving the *uncinate region* are characterized by peculiar epileptiform fits The aura of the seizure is often a sensation of smell or taste and is frequently although *not always an unpleasant one* The patient then passes into a peculiar dreamy state and this is followed by tasting or chewing movements If the visual fibers have been implicated crude visual hallucinations may occur in these attacks which may end in a generalized fit

Implication of the *postcentral gyrus* and *parietal lobe* is characterized chiefly by loss of sense of position point discrimination and localization and a disturbance of stereognostic perception The other forms of sensation such as pain touch heat and cold are little if at all affected Implication of the *left supramarginal gyrus* may produce apraxia and of the *left angular gyrus* word and letter blindness (alexia) If a lesion of this area such as tumor grows forward motor symptoms may be produced if downward into the subcortical region the

all right,' 'oh pshaw,' and 'oh boy, oh boy.' Another patient could say nothing but his name, which he would repeat over and over in a sing-song voice. This man could also carry the tune of a song, due probably to an intact singing center (?). The ability to write may be and usually is preserved in motor aphasia, although the patient may have to learn to write with the left hand. The power of pantomime is also preserved in motor aphasia. In hysterical loss of speech the patient as a rule cannot say any words at all, and other evidence of hysteria will be present. Furthermore, during the second stage of etherization the hysteric with loss of speech will talk.

Involvement of Wernicke's zone or the posterior part of the first and second temporal convolutions on the left produces sensory aphasia, also called jargon aphasia and Wernicke's aphasia. Implication of this particular part of the cortex produces word deafness. The patient is unable to understand perfectly what is said to him, although his hearing is normal. The words are as strange to him as though they were part of a foreign language; he cannot obey commands. In a pronounced type of word deafness he will be unable to follow a simple request such as 'put your right hand on top of your head.' On the other hand, the word deafness may be so slight that the patient fails only when given a number of commands at *once*, as *for example*, 'walk over to the door, open it, take off your coat and shake hands with me.' He must not be shown what to do. He is often unable to name a common object such as a knife or handkerchief which is shown him, although he may be able to use the object perfectly well. *Because of his word deafness he is* unable to write from dictation or to appreciate mistakes in speaking which he makes. Unlike the motor aphasic who suffers from a paucity of words, the sensory aphasic has plenty of words which he uses in a jargon. Lesions in the word hearing center are frequently *complicated by cuts in the* visual fields, due to involvement of the optic radiation.

*In mixed aphasia, the defect involves both* the patient's ability to express himself and to comprehend what is said to him.

In amnesic aphasia, the patient loses the ability to recall the names of common objects (amnesia), although he can describe the object and recognize the correct name when it is furnished to him. This form of aphasia results from a disturbance in language formulation. The lesion in such cases probably involves the dominant hemisphere in the area of the posterior part of the angular gyrus and the posterior part of the third temporal convolution.

*Visual aphasia* (*word blindness—alexia*) is due to a lesion of the dominant angular gyrus and produces a condition in which the patient can see words, letters and symbols but cannot interpret them. Here again it is as though he were gazing at a page written *in a foreign language*. Visual aphasia may vary from slight interruption to a complete loss of ability to name letters and words. He cannot copy sentences. Defects of the visual fields and parietal lobe symptoms may occur on the opposite side if the lesion extends beyond the angular gyrus. Involvement of all functions which go to make up speech produces *global aphasia*.

*Apraxia* is the inability to perform simple purposeful movements with the extremities when those parts show no loss of power or sensation and no ataxia. Apraxia may be ideational, ideomotor or motor. In the first, the ideas necessary to carry out an act are inadequate, resulting in a nonsensical act. Such a patient may, if given a cigarette and a match, put the match in his mouth and strike the cigarette. This type usually occurs in diffuse cerebral disease. In the ideomotor type, the association pathways between the ideational and motor kinesthetic centers are interrupted. The patient may show amorphous movements, may use the wrong gesture or the wrong muscle group. This is seen in lesions of the corpus callosum and in those which sever connections between the pre- and post-central gyri and other essential parts of the brain. Motor apraxia is produced by a subtotal lesion in a motor area of any extremity, resulting in an awkward movement, whereas the patient

In addition, certain cranial nerves especially the ninth and tenth may be involved Horner s syndrome may occur from involvement of the descending sympathetic tract

*Cerebellum* —The usual lesion in this structure is a tumor The symptoms produced are ipsilateral and consist of asynergia hypotonia and weakness, which is not however, of pyramidal tract origin but is due to the decreased muscle tone Alteration in the finger-to-nose test, the Holmes rebound phenomenon, a widened base of support and nystagmus occur in cerebellar lesions The gait is ataxic and reeling is not affected by closure of the eyes and the patient has a tendency to deviate to the side of the involvement The reflexes are reduced or lost and asthenia may be so pronounced as to simulate paralysis Involvement of the cerebellar peduncles may also produce cerebellar symptoms

*Cerebellopontile Angle* —This is a common location for neoplasms and inflammatory reactions especially syphilis The common tumor is one growing from the sheath of the eighth nerve producing tinnitus deafness and rarely dizziness Other cranial nerves especially the fifth and seventh may be implicated When the fifth is involved, symptoms simulating trigeminal neuralgia may occur but are differentiated by the sensory loss on the affected side The seventh nerve may be paralyzed but irritation of it may produce facial hemispasm or fits of twitching comparable to Jacksonian epilepsy Cerebellar symptoms and signs of increased intracranial pressure then ensue

*Pituitary Gland (Hypophysis)* —The gland may be the seat of atrophy or enlargement but the common lesion is a neoplasm which produces bitemporal hemianopsia This however may be preceded by minor visual field defects Choked disk in pituitary tumor is most uncommon but primary optic atrophy is frequently seen due to direct pressure on the chiasm Frohlich s syndrome may occur Pituitary basophilism has been described by Cushing its symptoms are adiposity involving the face neck and trunk amenorrhea and hypertrichosis in females hypertension hyperglycemia and bluish striæ in the skin Softening of the bones of the skeleton is a rare finding The syndrome occurs most frequently in young adults Roentgen ray evidence of involvement of the sella may be found

## APHASIA

Stewart defines aphasia as impairment or loss of speech due to the loss of memory for those signs vocal or written by means of which we exchange ideas with our fellow men The cortical centers which have to do with speech are on the left side of the brain in a right handed individual and on the right side in a left handed individual There are three important cortical areas concerned with speech namely the lower part of the third left prefrontal, which is the area for motor speech or Broca s area, the posterior part of the first and second temporal convolutions which has to do with word hearing and sensory speech and is sometimes called Wernicke s zone and the angular gyrus in which are stored images for words letters figures and signs Exact and precise localization of important functions in the cortex is denied by some especially Marie Aphasia is usually classified on the basis of the predominant defect as *(a)* motor or expressive *(b)* sensory or receptive *(c)* mixed and *(d)* amnesic Pure types of aphasia are very rarely encountered

Motor aphasia is caused by a lesion of Broca s area Because of the proximity of the face tongue and hand centers to Broca s area lesions of the latter will often implicate cortical motor centers and produce segmental cerebral monoplegia In motor aphasia the patient has lost the power partially or completely to express himself in spoken words The extent of the aphasia will vary with the severity of the lesion He may have slight difficulty with speech or if the lesion is extensive speech may be entirely lost If the disturbance of speech is slight and mistakes are made the patient usually recognizes them While the patient may be speechless he is practically never wordless but has a recurring utterance which he will use either spontaneously or in reply to questions Expressions of some patients who have recurrent utterances are as follows

anyone any I know I know I know

the artery of cerebral apoplexy. The result *of occlusion of this vessel or of the middle* cerebral produces the commonest condition seen as the result of vascular injury, namely *hemiplegia*. The ordinary type of hemiplegia is more frequent in men, and usually occurs after the age of forty or forty-five years. If a stroke occurs before forty it is imperative that such disorders as syphilis, embolism, vascular anomalies, brain abscess, cerebral tumor and encephalitis be ruled out as the causative factor.

The usual location of hemorrhage or softening is in the region of the internal capsule. The size of a hemorrhage may vary greatly from a small lesion to a large one which may involve a great part of the cerebral *hemisphere and which may ultimately* rupture into the ventricles. If the patient dies shortly after a cerebral hemorrhage has occurred the lesion will have the appearance of freshly coagulated blood; later it goes through various color changes and a cyst or cavity remains. The apoplectic seizure may be initiated by injury, may come on as the result of severe muscle exertion such as the exertion of paroxysmal coughing as occurs in whooping cough, straining at stool during coitus, parturition or any severe muscular effort. Many cases of apoplexy *occur in patients with low blood* pressure. The *apoplectic seizure* may be preceded by certain premonitory symptoms such as numbness on the side of the body about to be paralyzed, headache, dizziness, *vomiting, convulsions or confusion.* Many patients have been conscious for months or years that they are the victims of high blood pressure and kidney disease, but on the other hand others feel in normal health. Physical overexertion and anxiety may apparently produce a cerebral attack in middle age and in supposedly healthy individuals.

*Symptoms.—Immediately after* a vessel has been damaged the patient usually becomes comatose, although occasionally consciousness is completely retained. In a patient who has a cerebral hemorrhage the onset is more rapid and the coma deeper than in a patient with thrombosis. The case of cerebral hemorrhage is very ill from the start. The breathing is stertorous and at times of the Cheyne-Stokes type. The face is flushed, the pupils may be small, normal *or dilated, and are frequently* unequal. The corneal reflexes are abolished, the individual is shocked, all the extremities are likely to be flaccid, the deep reflexes especially on the side of the paralysis may be absent. The plantar reflex will practically always be of the extensor type on the paralyzed side, even though the deep reflexes are lost. Despite the fact that all the extremities are flaccid and drop helplessly to the side when they are lifted from the bed, those on the paralyzed side are much more toneless than those on the other. In the stage of shock *swallowing is impossible and the* control of the sphincters is lost. Some degree of fever occurs soon after the onset. *Steadily rising temperature* is a bad prognostic sign. Later on the presence of fever may be due to pneumonia. If the urine is examined it will frequently be found to show evidence of nephritis or of diabetes; however sugar may be found in the urine as the result of a cerebral lesion alone. If the hemorrhage ruptures into the ventricles the patient becomes extremely ill and signs of meningeal irritation occur. The picture of decerebrate rigidity may present itself in patients with hemorrhage into the ventricles. Pyramidal tract signs are bilateral. Pronounced respiratory *difficulties ensue, the pulse slow at* first becomes rapid, the temperature may become subnormal or high, and the patient dies, as a rule, within two to seven days. Lumbar puncture reveals a bloody fluid.

*The onset in cerebral thrombosis is usually* not so abrupt, premonitory symptoms are more commonly seen, the patient is not so severely shocked, stupor if present is not as deep as in hemorrhage. Furthermore, partial paralysis may exist a number of hours, even a week or more before becoming complete. This is especially so when the *artery in the Sylvian fissure is involved.* Cerebral embolism which usually results from heart disease, particularly subacute endocarditis, may resemble thrombosis, but the onset is usually sudden. The diagnosis is based on the heart findings and in some cases the finding of a positive blood culture. The retinal vessels will usually show arteriosclerosis and rarely the optic nerves show signs of neuritis or of choking.

formerly was able to carry out fine movements with the same part.

In the differential diagnosis aphasia of the sensory type and agnosia must be ruled out as well as extrapyramidal movements such as are seen in chorea and athetosis.

*Agnosia* may be defined as a loss of the ability to recognize objects in the absence of any impairment of the perceptive functions of the sense organs. In auditory agnosia (psychic deafness) the patient is unable to identify auditory stimuli; for example, with his eyes closed he cannot identify a dog by its bark or a bell by its tinkle. This is due to a disturbance in the association fibers connecting the auditory sensory center in the temporal lobe with the conceptual center in the frontal lobe. Often there is an accompanying sensory aphasia. In visual agnosia (psychic blindness), the patient loses the understanding of the significance of an object. For example, he may describe a knife accurately but can not recognize what it is. This occurs in lesions involving the convexity of the occipital lobe. Tactile agnosia or astereognosis, as previously noted, occurs with lesions of the postcentral gyrus.

The testamentory capacity of patients suffering from various forms of aphasia is often brought up. The uncomplicated cases of motor aphasia will usually have testamentory capacity and a disposing mind. By talking with such an individual his will and desire can be appreciated. On the other hand, it is impossible to communicate sufficiently with the patient suffering from sensory aphasia to know what disposition of his property he might wish to make, and there is a question if wills made by such patients should be allowed to stand.

## DISORDERS OF ARTICULATION

Articulation has nothing to do with cortical functions but is a function of the bulb and the peripheral mechanisms. A patient with advanced bulbar palsy or pseudobulbar palsy may be unable to put forth a single word, yet he is not speechless. Difficulty in articulation is spoken of as dysarthria and is common for example in pseudobulbar palsy. If the disturbance of articulation is advanced it may render the patient unable to say a word or make a sound. This is called *anarthria*. Involvement of articulation may be due to lesions of the cranial nerves or their nuclei which have to do with speech, to supranuclear involvement as in pseudobulbar palsy, or to incoordination of the muscles of the lips, tongue, palate, pharynx and larynx. A slurred type of speech is common in alcoholism and paresis. Sometimes the speech of multiple sclerosis may be slurred and simulate that of general paresis. Tremor or involuntary movements affecting the movements of articulation may produce *dysarthria*. In paralysis agitans the voice is monotonous and often has a festinating character. The most common type of speech disturbance is stammering. This is most frequently found in males who are usually above the average intelligence and are frequently of a psychasthenic makeup. *Stammering* is an incoordination between the vocal and oral mechanisms of speech, and the stammerer frequently sticks on an initial consonant or syllable. Stammering is usually increased by excitement and for the most part disappears when the stammerer sings. Most stammerers acquire certain tricks which aid them to overcome their speech defect; they most commonly make certain grimaces or quick tic-like movements of the body or the extremities. These are often not unlike the tic movements which the psychasthenic shows. When stammering appears it should be treated by exercise and speech training. While the child may grow out of it, he will certainly do so more quickly if he has the proper training.

*Hysteria may produce certain disturbances* in articulation in which the voice may be entirely lost or the patient can speak only in a whisper. *Hysterical mutism* may or may not be accompanied by paralysis, and the patient can always write.

## DISEASES OF THE BLOOD VESSELS OF THE BRAIN

*Etiology.*—The commonest condition affecting the blood vessels of the brain is arteriosclerosis, which may be part of the generalized disease, or it may be limited to the vessels of the brain. Vessels which are diseased by arteriosclerosis may give rise to a cerebral hemorrhage; they may thrombose, causing secondary softening beyond the point of the lesion; or the cerebral vessels may be the site of aneurysms. On the other hand, a cerebral vessel may be plugged up with an embolus, or it may be implicated by aneurysm produced by the lodging of microorganisms in its wall with subsequent weakness and dilatation. Any vessel of the brain may be the site of vascular insult, but the lenticulo-striate artery is so *frequently involved that it has been called*

out the production of symptoms referable to the entire cortex supplied by the artery

In considering the *differential diagnosis* of apoplexy it is necessary to consider all of the causes which may produce stupor or coma Of 200 cases with coma 83 had skull fractures 53 apoplexy, 12 uremia, 10 lobar pneumonia, 8 meningitis and 6 diabetic coma In the rest it was due to scattered causes In other studies cerebral hemorrhage has been shown to be the most common medical cause of coma (excluding trauma and alcoholism) There is no doubt of the frequency with which *uremia* is overdiagnosed A great tendency exists to label a patient unconscious, with paralysis of one side and with albumin and casts in the urine as a uremic hemiplegic As a matter of fact such cases are most often due to cerebral hemorrhage *Injuries to the head*, especially those persons who suffer cerebral hemorrhage without fracture can usually be differentiated by the history *Diabetic coma* can be determined by the analysis of the blood and urine but it must be remembered that cerebral lesions may produce glycosuria The diagnosis between *apoplexy* and *postepileptic stupor* can be made in some cases by the record and by the absence of paralysis although the plantar reflex may be of the extensor type due to cortical exhaustion after a fit Further more scars may be found upon the face and tongue of the epileptic and he may have the facies peculiar to those people In some cases an exhaustion paralysis occurs after a series of epileptic fits especially if they are unilateral On the other hand an epileptic may rupture a cerebral vessel (either intra or extracerebral) during a spasm and a hemiplegia will result *Hysterical hemiplegia* is differentiated by the absence of abnormal reflexes loss of sensation often exists on the paralyzed side hearing and vision may be affected on the paralyzed side other symptoms suggestive of hysteria may be detected Alcoholic coma can be diagnosed by the history of the individual the usual absence of pathologic reflexes and of paralysis and the tendency toward delirium and restlessness Because of the ease with which such *drugs* as the barbiturates are obtained patients are not infrequently seen in coma produced by the overuse of those drugs In the absence of the history therefore the diagnosis is difficult Hematoporphyrin in the urine may give an important clue in patients comatose from such drugs as veronal *Hyperinsulinism* may produce coma and be accompanied by bilateral pyramidal tract signs (*See* Chapter 15) Spontaneous *subarachnoid hemorrhage* may induce stupor and because of the presence of blood in the spinal fluid may be confused with cerebral hemorrhage with rupture into the ventricles However in the latter the patient is always much sicker than in the former is more deeply stuporous and will show more extensive paralysis A patient suffering from a *brain tumor* may have a hemiplegia of apoplectic suddenness due to hemorrhage into the tumor The possibility of brain tumor is often not thought of in such cases, but examination of the eye grounds and estimation of the spinal pressure will help in the diagnosis

*Treatment* —The most important thing under this heading is prophylaxis For this the reader is referred to the article on arteriosclerosis In the acute attack the patient must necessarily be put to bed the head should be slightly elevated An olive oil or a simple enema should be given immediately

Owing to the frequency with which hypostatic pneumonia develops penicillin or some other antibiotic should be administered and the patient should be kept off his back and on the paralyzed side as much as possible The position should be changed frequently An air mattress or water mattress should be used to prevent the occurrence of trophic sores An ice bag to the head sedatives for great restlessness and absolute cleanliness of the skin are important considerations in the treatment If swallowing is either impaired or impossible great care should be used in giving the patient food or liquids by mouth For the first two or three days it is better to give liquids by rectum or with a nasal tube rather than to run the risk of having the patient aspirate it into the lungs The treatment is chiefly symptomatic In cases of cerebral thrombosis immediate stellate block ipsilateral to the lesion has been advocated to relieve cerebral vasospasm

It is our experience that those cases of hemiplegia associated with *choked disks* are usually due to cerebral neoplasm A conjugate deviation of the eyes, usually toward the side of the cerebral lesion may be seen Most patients with cerebral hemorrhage die A patient with cerebral thrombosis has a much better *chance to survive If he does he will then present the picture* of a hemiplegia, that is, paralysis or weakness of one side of the body with contractures and the signs of pyramidal tract disease

*Sensation* is not affected in the ordinary case of hemiplegia, unless the thalamus or the posterior limb of the capsule is involved *pain on the paralyzed side is due to thalamic* irritation or to joint disease which is especially likely to occur in the shoulder Early in the history of the case the patient s *speech* will be dysarthric or even absent If the dominant cortex has been involved speech may be greatly affected and either motor or *sensory aphasia or both exist*

Many patients suffering from cerebral vascular disease die within a few weeks others recover enough power on the affected side to permit their getting up and around The lower extremity recovers more power than the upper and the proximal segments of the *upper extremity regain more strength* than the distal ones In walking the hemiplegic patient swings the entire lower extremity on the affected side from the hip the knee is *held rigidly and the toe is scraped* along the floor The arm is slightly abducted the elbow usually flexed to a right angle the hand *is pronated* and bent and the fingers are flexed Often the hand on the paralyzed side is carried across the lower part of the abdomen although occasionally it is held in extension at the side *Contractures* will occur unless attention is directed to their prevention If the paralysis remains a *flaccid one*, the patient will not as a rule recover function Atrophy may occur on the paralyzed side and may be due to inactivity and to ankylosis *Electrical reactions* remain normal In a lesion of the thalamus or posterior limb of the capsule all forms of sensation may be seriously affected hemianopsia may occur and the paralyzed or weak limbs may be the site of disagreeable sensations or actual pain Pain on the paralyzed side may be produced, especially *in a lesion of the thalamus, by testing* the patient for sensation, thus, the application of a piece of ice, an extremely hot test tube or deep pressure on the paralyzed side or scratching it with a pin may provoke an abnormal response, which has *been referred to as dysesthesia* While this is characteristic of disease of the thalamus it may occur from irritation, to the sensory pathways in other parts of the central nervous system

*Trophic disorders* may occur on the paralyzed side in the joints, skin or nails and muscular atrophy may be due to trophic disturbances or to joint disease Occasionally one sees hemiplegia which, after a few hours' duration, clears up suddenly This may be due to a spasm of the cerebral vessel Hemiplegia of short duration is a common happening in general paresis

If the carotid artery is thrombosed before *it gives off the ophthalmic artery, there is* blindness on the side of the lesion and a hemiplegia on the opposite side

Even in the most favorable case a certain amount of reduction in the *mental faculties* of the individual ensues If the lesion has been a large one and especially if bilateral changes caused by arteriosclerosis are present mental changes may occur varying from acute psychosis to a severe dementia Vascular disease involving the pons or *medulla may occur These usually produce* a crossed paralysis Hemorrhage into the pons sometimes occurs in brain abscess or tumor or in other conditions producing increased pressure and frequently causes sudden death

Occlusion of the branch of the anterior cerebral artery supplying the foot and leg center will cause a *monoplegia* of the lower extremity on the opposite side to the lesion Occlusion of the Sylvian artery is not an infrequent occurrence and if the *left Sylvian* artery be involved a devastating group of symptoms ensues because of implication of the special centers located on the left side of the brain Any one of the branches of the Sylvian artery may become affected without involvement of the entire artery motor aphasia sensory aphasia alexia parietal lobe symptoms or paralysis may ensue with

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The block must be repeated frequently and is of little or no value if the hemiplegia has existed for more than a few hours While encouraging results have been reported by a few investigators our own experience has not been so favorable Stellate block is contraindicated in cerebral hemorrhage At present this method of treatment should still be considered as being in the experimental stage

Since the cerebrovascular accident frequently occurs as a manifestation of systemic circulatory failure, therapy directed toward improving the general circulation should be instituted

If the patient survives to become a hemiplegic the paralyzed limb should be given massage and passive movement These forms of physiotherapy should be employed early in the case certainly by the end of the first week, otherwise the tendency toward contractures and joint changes will be great Electricity is chiefly of psychotherapeutic value Rarely orthopedic operations, may be employed Aphasia if present, may improve spontaneously but it is usually necessary to attempt to reeducate the individual

## SPONTANEOUS SUBARACHNOID HEMORRHAGE

Spontaneous subarachnoid hemorrhage is not uncommon At the Philadelphia General Hospital it was found in nearly 2 per cent of all brain autopsies Almost invariably it results from the rupture of a miliary or berry aneurysm of the circle of Willis These aneurysms are due to a congenital defect in the media and are invariably located at the point where the artery gives off branches In a series of 45 cases reported by Wilson, Rupp and Bartle 17 occurred in the internal carotid artery 16 on the anterior communicating, 5 on the middle cerebral, 2 each on the anterior cerebral and basilar arteries and one each on the posterior cerebral posterior inferior cerebellar, and superior cerebellar arteries respectively Trauma syphilis and arteriosclerosis are not important as etiologic factors The exact cause of the rupture of these aneurysms is not known but a close parallelism exists between these cases and those showing a primary intracerebral hemorrhage in respect to age incidence elevation of blood pressure and the presence of concomitant cardiac vascular disease

*Symptoms*—Spontaneous subarachnoid hemorrhage may occur at any age The average age in the cases reported by us was forty four years The onset is usually abrupt but may be insidious In some cases the hemorrhage may follow severe activity or emotional excitement while in many cases there is no discernible precipitating cause The patient may first complain of severe headache and dizziness and fall to the ground Coma psychic disturbances such as confusion excitement and hallucinations and convulsions may be present Nuchal rigidity and Kernig s signs are almost always present The pupils may be unequal extra ocular muscle palsies and other evidence of cranial nerve dysfunction may be noted Hemiplegia or hemiparesis not infrequently are found The tendon reflexes vary greatly they may be increased or in some cases decreased Babinski s sign is sometimes seen on one side or both If the patient is not completely stuporous he will probably complain of a severe headache associated perhaps with vomiting The eye grounds may reveal swelling and retinal hemorrhages may occur The pulse and respiration may be slow or rapid depending upon the intracranial pressure and shock and a moderate rise of temperature frequently exists Glycosuria and hyperglycemia have been found at times and may lead to an erroneous diagnosis of diabetic coma At first the spinal fluid is bloody and the pressure increased later the fluid becomes xanthochromic

*Diagnosis*—The diagnosis of spontaneous subarachnoid hemorrhage should be considered as a possibility in any patient in stupor The history of sudden onset the signs of meningeal irritation and the presence of blood in the spinal fluid suggest the diagnosis Recovery occurs in about 50 per cent of the cases but later there may be another rupture which may prove fatal The aneurysm may frequently be visualized by angiography

*Treatment* —In the acute stage therapy is largely symptomatic The general circulatory status should not be neglected and any therapy which might increase its efficiency should be instituted If the patient is restless, sedatives such as paraldehyde by rectum or sodium phenobarbital hypodermically should be administered Morphine is contraindicated An ice bag to the head may be comforting if headache is severe Repeated spinal punctures are not recommended unless headache is quite severe, persistent and cannot be alleviated by other means since fresh bleeding may cause death Occasionally other methods of reducing increased intracranial pressure such as magnesium sulfate enemas and hypertonic intravenous solutions may be used If the patient survives the acute manifestations surgical procedures to prevent further bleeding may be justified In some cases the aneurysm may be clipped intracranially in others, tying the carotid artery on the side of the aneurysm may be considered These procedures are not without danger and therapy must always be individualized

## SINUS THROMBOSIS

The various sinuses of the brain may be occluded either as the result of infection or as a terminal state in such conditions as tuberculosis paresis cardiac disease, pregnancy and after any long standing debilitating disease The type of sinus thrombosis produced by infections may be complicated by meningitis or brain abscess and also by extradural collections of pus The sinus most frequently involved is the lateral sinus which is affected secondarily to disease of the ear The cavernous sinus may be implicated by infections about the face especially those on the upper lip and about the tip of the nose Fortunately the incidence of these serious complications has been greatly reduced since the advent of the antibiotics The common cause of thrombosis of the superior longitudinal sinus is long standing illness

The sinus thrombosis may be localized or may be very extensive especially in the type produced by infections The walls of the sinus may be eroded and death occur suddenly from hemorrhage Cerebral hemorrhage may occur, especially when the superior longitudinal sinus is thrombosed because the brain cannot properly be drained of blood, and hyperemia and bleeding ensue

*Symptoms* —Symptoms of occlusion of the superior longitudinal sinus are as follows signs of increased intracranial pressure are present often accompanied by paralysis which is due, as a rule, to cortical bleeding Generalized or Jacksonian convulsions may occur Signs of meningitis may be present

Thrombosis of the cavernous sinus produces swelling of the eyelids on the affected side swelling at the root of the nose exophthalmos and as a rule paralysis of all the ocular nerves on that side Visual disturbances are common and there may be choking of the disk Implication of the ophthalmic division of the fifth nerve may cause pain in its distribution The opposite cavernous sinus may be involved secondarily Thrombosis of the sigmoid or the lateral sinus may produce a swelling at the upper part of the jugular vein which may be palpated Swelling in the mastoid region signs of meningitis and occasionally paralysis of the lower cranial nerves on the affected side may be discovered A modification of the Queckenstedt test the Tobey Ayer test may produce valuable evidence in lateral sinus thrombosis In this test the pressure on the jugular vein on the normal side causes a rise in the spinal pressure whereas if the jugular vein is thrombosed there will be no rise Occasionally in cases of infections of the ear the so-called *Gradenigo syndrome* may be present The chief symptom of this is a paralysis of the sixth nerve on the side of the lesion and occasionally symptoms indicative of implication of the sensory part of the fifth nerve These symptoms may be due to an aseptic meningitis which may quickly disappear there is however always cause for alarm in the possibility of meningitis or abscess Petrositis is a complication of middle ear disease The acute symptoms are signs of sepsis periauricular pain interference with movements of the lower jaw, these may be followed by chronic suppuration of the petrous tip with pain in and around the eye and *Gradenigo s syndrome* Vertigo and

The block must be repeated frequently and is of little or no value if the hemiplegia has existed for more than a few hours. While encouraging results have been reported by a few investigators, our own experience has not been so favorable. Stellate block is contraindicated in cerebral hemorrhage. At present, this method of treatment should still be considered as being in the experimental stage.

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If the patient survives to become a hemiplegic, the paralyzed limb should be given massage and passive movement. These forms of physiotherapy should be employed early in the case, certainly by the end of the first week; otherwise the tendency toward contractures and joint changes will be great. Electricity is chiefly of psychotherapeutic value. Rarely orthopedic operations may be employed. Aphasia, if present, may improve spontaneously, but it is usually necessary to attempt to re-educate the individual.

## SPONTANEOUS SUBARACHNOID HEMORRHAGE

Spontaneous subarachnoid hemorrhage is not uncommon. At the Philadelphia General Hospital it was found in nearly 2 per cent of all brain autopsies. Almost invariably it results from the rupture of a miliary or berry aneurysm of the circle of Willis. These aneurysms are due to a congenital defect in the media and are invariably located at the point where the artery gives off branches. In a series of 45 cases reported by Wilson, Rupp and Barthe 17 occurred in the internal carotid artery, 16 on the anterior communicating, 5 on the middle cerebral, 2 each on the anterior cerebral and basilar arteries, and one each on the posterior cerebral, posterior inferior cerebellar, and superior cerebellar arteries, respectively. Trauma, syphilis and arteriosclerosis are not important as etiologic factors. The exact cause of the rupture of these aneurysms is not known, but a close parallelism exists between these cases and those showing a primary intracerebral hemorrhage in respect to age incidence, elevation of blood pressure and the presence of concomitant cardiac vascular disease.

*Symptoms.*—Spontaneous subarachnoid hemorrhage may occur at any age. The average age in the cases reported by us was forty-four years. The onset is usually abrupt but may be insidious. In some cases the hemorrhage may follow severe activity or emotional excitement, while in many cases there is no discernible precipitating cause. The patient may first complain of severe headache and dizziness and fall to the ground. Coma, psychic disturbances such as confusion, excitement and hallucinations, and convulsions may be present. Nuchal rigidity and Kernig's signs are almost always present. The pupils may be unequal; extra-ocular muscle palsies and other evidence of cranial nerve dysfunction may be noted. Hemiplegia or hemiparesis not infrequently are found. The tendon reflexes vary greatly; they may be increased or in some cases decreased. Babinski's sign is sometimes seen on one side or both. If the patient is not completely stuporous he will probably complain of a severe headache, associated perhaps with vomiting. The eye grounds may reveal swelling, and retinal hemorrhage may occur. The pulse and respiration may be slow or rapid, depending upon the intracranial pressure and shock, and a moderate rise of temperature frequently exists. Glycosuria and hyperglycemia have been found at times and may lead to an erroneous diagnosis of diabetic coma. At first the spinal fluid is bloody and the pressure increased; later the fluid becomes xanthochromic.

*Diagnosis.*—The diagnosis of spontaneous subarachnoid hemorrhage should be considered as a possibility in any patient in stupor. The history of sudden onset, the signs of meningeal irritation and the presence of blood in the spinal fluid suggest the diagnosis. Recovery occurs in about 50 per cent of the cases, but later there may be another rupture which may prove fatal. The aneurysm may frequently be visualized by angiography.

plasm which often spreads through the subarachnoid space and occurs most frequently in the mid line of the cerebellum in children This type of tumor can be held in check for a time by radiation An oligodendroglioma is a slowly growing tumor which usually arises from the cortex and often becomes calcified It is most common in the early thirties of life Gliomata are usually single and are frequently the site of degeneration and hemorrhage

*Endothelioma* (fibroblastoma, meningioma) is a relatively benign tumor which usually arises from the arachnoid villi and may occasionally become calcified when it is called a psammoma It occurs most commonly in the middle years of life A large majority are found in the anterior two thirds of the skull They may be found close to the falx in the midline in the Sylvian fissure and on the sphenoidal ridge in the olfactory groove tuberculum sellae or parasellar regions Less commonly they are found on the petrous ridge or in the posterior fossa Fibroblastomata may produce hyperostosis of the cranium or occasionally thinning or even erosion of the bone

*Acoustic fibromata* or *neuromas* are benign circumscribed growths growing from the dural sheath of the eighth nerve They may occur as bilateral angle tumors

*Tuberculomas* may be single or multiple usually the latter and are often secondary to tuberculosis elsewhere in the body although sometimes no other tuberculous focus can be detected They usually have a connective tissue capsule and frequently central caseation occurs Rarely the tubercle becomes calcified and does not produce symptoms A diffuse tuberculous meningitis is often a common end result of a tuberculoma They are found in adults as well as in children grow slowly and occur thoughout the cortex cerebellum and brain stem

*Gummata* are rare and usually multiple

*Adenomata* occur in the pituitary gland and are extremely important in relation to acromegaly and Frohlich s syndrome

*Sarcomata* are either primary or secondary and single or multiple They usually grow from the meninges into the brain and may be encapsulated or invasive They may be secondary from sarcomata elsewhere in the body *Other tumors* such as cholesteatoma dermoid cysts and teratomata are rare

*Carcinomas* are always secondary grow rapidly are usually multiple and quite vascular The presence of carcinoma elsewhere in the body should always be ruled out before operating upon a brain tumor suspect This is especially important when a person is above the age of forty years as sometimes the intracranial manifestations may be the earliest evidence of carcinoma

*Angiomata* arise from the blood vessels of the meninges and may be associated with birthmarks on the scalp or face Angiomata are especially likely to be seen in the precentral region *Lindau s disease* consists of angioma of the brain and angiomatosis of the retina

The *cause* of brain tumors is unknown Their relation to trauma is a most important one especially from a medico-legal aspect Endotheliomata undoubtedly sometimes follow trauma The general symptoms of a brain tumor may be abruptly brought on by head injury but it is extremely doubtful if the tumor itself can be produced by trauma

*Symptoms* —The expressions of brain tumors are both general and focal The most constant symptom is headache and while it may be occasionally absent it practically always occurs sometime in the history of the case Severe *headache* especially if associated with dizziness and vomiting should always arouse suspicion of a cerebral neoplasm The headache is usually generalized but may be located either in the occipital or frontal regions when it may be associated with local tenderness Headache is due to stretching of the dural blood vessels *Choked disk* or papilledema is a frequent sign of brain tumor but may not occur until late in the course The presence of choked disk indicates a brain tumor in at least 90 per cent of cases and the burden of the proof is on him who propounds another diagnosis Choked disk is most frequently seen with tumors which block the ventriculo subarachnoid pathways and cause increased ventricular pressure it is an extremely common sign in tumors in the posterior fossa Papilledema is usually bilateral but frequently is more pronounced on one side A

nystagmus may be seen in the chronic form Paralysis of the seventh nerve may take place, and other cranial nerves may be implicated The condition may subside or meningitis or brain abscess follow

Signs of meningitis make it imperative to perform a lumbar puncture Only enough fluid should be withdrawn, however to determine the color and transparency to count the cells and make a smear for organisms The fluid may contain an excess of cells and no organisms

The outlook in cases of sinus thrombosis is serious Penicillin sulfa compounds and other antibiotics should be given immediately Septic foci must be drained surgically Ligation of the facial vein may be employed as a prophylaxis against the involvement of the cavernous sinus

## CEREBRAL ANEURYSM

Cerebral aneurysms are most frequently congenital in origin and are due to defects in the development of the cerebral blood vessels Most common are the miliary type which are found at the base of the brain at the points of bifurcation of branches of the arteries composing the circle of Willis Occasionally congenital arterio-venous aneurysms are present Rarely the aneurysms are of infectious (embolic) origin or are the results of syphilitic or arteriosclerotic involvement of the vessels The arteries at the base of the brain are more frequently involved and aneurysms are likely to be multiple They are usually small but occasionally attain a fairly large size before rupturing The parts of the brain in the immediate vicinity of a cerebral anerurysm may undergo a pressure atrophy Trauma may play a role in the production of a cerebral aneurysm and it is certain that sufficient trauma can cause the rupture of a cerebral aneurysm already present

Before the rupture occurs the aneurysm may produce *symptoms* such as headache often referred to the side on which it exists vomiting and dizziness A murmur may be heard over the skull This may be localized or heard over a widespread area A murmur may also be detected over the skull in rickets, hydrocephalus hyperthyroidism and occasionally over a neoplasm General signs of increased pressure are rarely found If an aneurysm ruptures, which it may do either spontaneously or as a result of trauma or severe muscular effort a massive hemorrhage may occur Slow bleeding may take place into the subarachnoid space If the aneurysm is near the ventricular system and ruptures into it signs of intraventricular hemorrhage will exist Aneurysms of the large vessels of the brain other than those at the base will produce symptoms referable to the parts of the brain involved The optic and olfactory nerves may be compressed by an aneurysm of the anterior cerebral artery and an aneurysm of the internal carotid may affect the ocular nerves in addition to the optic and olfactory and even occasionally the fifth If the aneurysm perforates into the cavernous sinus pulsating exophthalmos may occur

The *diagnosis* of cerebral aneurysm is sometimes difficult but if suspected confirmation may usually be obtained by angiography In a patient suffering from subarachnoid bleeding non traumatic in origin it is fair to assume the hemorrhage has been due to the rupture of a small aneurysm The treatment in general is that of subarachnoid hemorrhage and of cerebral hemorrhage Surgical intervention may be helpful

## *BRAIN TUMORS*

Brain tumors comprise from 1 to 2 per cent of all neurologic disorders The tumor may be primary in the brain and its appendages or metastatic from a neoplasm elsewhere in the body

*Pathology* —The most common brain tumors are *gliomas* which comprise from 40 to 50 per cent of all intracranial neoplasms Various types of glioma are to be distinguished Glioblastoma multiforme (gliosarcoma—spongioblastoma multiforme) is usually seen in middle life occurs in the hemispheres is malignant and attains large size An astrocytoma is more benign has a tendency to become cystic and may involve the cerebrum or cerebellum It occurs usually in children or in young adults A medulloblastoma is a rapidly growing neo-

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reasonable amount of antisyphilitic therapy the possibility of a nonspecific tumor should be suspected Hydrocephalus either acute or chronic may produce symptoms closely resembling those of a brain tumor The history and the usual absence of focal signs will help to clear up the diagnosis If a case of multiple sclerosis begins abruptly especially with visual changes optic neuritis and other focal signs, such as Jacksonian epilepsy it may be misdiagnosed and operated upon for brain tumor

*Roentgen Diagnosis* —L P Pendergrass of the University of Pennsylvania has kindly written the following

The roentgen examination of the head is extremely valuable in the diagnosis of tumors of the vault and of the brain Tumors of the vault can be easily demonstrated by the changes that occur in the bones that make up the skull such as fibroblastomas and osteomas Bone disease such as syphilis tuberculosis and fibrosing osteitis is also easily demonstrable and the appearance of these diseases is usually easily differentiated In diagnosing intracranial lesions there are two groups sellar and extrasellar One can diagnose a pituitary tumor in approximately 97 per cent of the cases and possibly the percentage may be increased when there is a correlation of clinical and roentgenologic findings The diagnosis of an extrasellar tumor is somewhat more difficult and depends upon several factors (1) Calcification within the tumor is seen in some gliomas endotheliomas Rathke s pouch tumors and rarely in tuberculoma (2) The changes in the dorsum sellæ are due to pulsation from a dilated third ventricle such as occurs in tumors involving the pineal the angle fourth ventricle and cerebellum In fact anything that will block the ventricular system will show ultimately an atrophy of the dorsum sellæ Another valuable sign is the displacement of the pineal body This may be of localizing evidence

The injection of air into the ventricles is a decided help in some cases *Encephalography* is a risky procedure in a brain tumor suspect and should under no circumstances be done if clinical and manometric signs of greatly increased pressure exist (*See* page 1405)

*Lumbar Puncture* —Whether or not a lumbar puncture should be done in patients suffering from cerebral neoplasm is a disputed point It is not as dangerous as some writers contend If the spinal tap is done carefully a small needle used and little fluid withdrawn and the pressure is not elevated above 200 mm of water, little danger will ensue to the patient The great risk of this procedure is in tumors in the posterior fossa Quite a few of these patients succumb suddenly due to respiratory failure Under no circumstances should a large amount of fluid be taken out if the spinal pressure is elevated but enough can be removed so that the important laboratory examinations on the fluid may be performed In a patient suspected of having a tumor and without choking an examination of the spinal fluid is indicated, not only for pressure but also for syphilis

Bárány Tests —Bárány tests are of great value in localizing lesions in the cerebellopontile angle or in saying that a tumor does not exist in that region Otherwise little help is obtained from these tests

Electroencephalography is occasionally of help in localizing the tumor particularly when the growth is superficially located Recent demonstration that intracranial neoplasms tend to concentrate radioactive substances injected into the body gives promise that another helpful and valuable diagnostic technique may be developing

*Treatment* —The treatment of brain tumors is surgical Brilliant results may be obtained especially when the lesion is growing from the brain coverings although most cases do poorly Roentgen ray treatment is of value in a small group The most important point in the treatment of an intracranial lesion suspected of being a tumor is to withhold operation, until the diagnosis is reasonably certain

## INJURIES OF THE BRAIN

In the analysis of a patient suffering from head injury it is important to know the following

1 The length of the period of unconsciousness

2 Whether paralysis or other localized cerebral symptoms existed

high degree of choked disk may be present without much loss in visual acuity, although, as a rule, the condition leads to changes in the visual fields, later impairment of vision, which may go on to blindness and secondary optic atrophy develops Blindness may occur suddenly Choked disk is extremely uncommon in tumors of the pituitary which produce, as a rule, primary optic atrophy *Vomiting* may occur at any time and is a particularly common symptom in the tumors of the posterior fossa, it is due to irritation of the centers in the medulla Vomiting is not as a rule, associated with nausea it has no relation to meals and may or may not be of the projectile type Hiccoughing is a rare symptom *Dizziness* as a symptom of brain tumor is frequently due to neoplasm in the posterior fossa and those which involve the vestibular pathways Sudden change of position may induce vertigo especially if the tumor is in the fourth ventricle

*Convulsions* may occur at any time in the history of a neoplasm Their occurrence after the age of twenty five or thirty years should arouse the suspicion of a brain tumor Attacks simulating petit mal loss of consciousness and status epilepticus may sometimes be seen in brain tumors Jacksonian fits and partial continuous epilepsy are of focal rather than general significance Disturbance in the rhythm of the pulse and respiration occur most frequently due to tumors in the posterior fossa and are due to medullary compression The pulse becomes slow and the respiratory rate is decreased even Cheyne-Stokes breathing may be seen Sudden respiratory failure is a fairly common cause of death in brain tumor and in such cases the heart may continue to beat for some time after respiration has ceased Mental changes occur as the general symptoms of brain tumor but have little localizing value

Alteration of the temperature which may be either subnormal or increased is a rare symptom of a brain tumor but hyperthermia may occur in tumors in the region of the third ventricle Glycosuria and diabetes insipidus are focal rather than general symptoms

*Localizing Symptoms* —It is important to record the symptoms and signs in the order of their development The earlier a symptom or sign appears, the more important it is from a focal standpoint Late appearing symptoms have to be largely discounted For example, the occurrence of a sixth nerve palsy early in the history of a brain tumor may have some importance as a focalizing sign but if it occurs late it may be and usually is due to general increase of intracranial pressure Sometimes a posterior fossa tumor produces symptoms referable to the frontal lobes and the exact reverse may occur It is not infrequent that well marked general symptoms of a brain tumor exist and few, if any, localizing signs are seen The onset of the general and localizing symptoms in a brain tumor are usually insidious but occasionally they may occur with epileptiform suddenness

Acute alcoholism and injury to the head often serve as the precipitating factor Cases of hemiplegia supposedly due to vascular disease, and associated with choked disk are often instances of brain tumors with sudden onset

The existence of choked disks is extremely important It occurs in at least 80 per cent of brain tumors and if present usually indicates a neoplasm Papilledema may also occur in sinus thrombosis sinusitis meningitis and encephalitis Unilateral choked disk may sometimes be seen on the side of a brain tumor On the other hand it may be due to focal infection Papilledema may occasionally be seen without the general symptoms of a brain tumor Careful studies of the visual fields often give valuable information and should never be neglected

*Diagnosis* —A slowly progressive hemiplegia due to thrombosis of the middle cerebral artery especially that part in the Sylvian fissure may prove troublesome in differentiating it from a brain tumor

Neurosyphilis should always be considered and ruled out before the patient is subjected to operation for brain tumor General paresis especially should be eliminated Occasionally a brain tumor may develop in a syphilitic who has positive laboratory findings in the blood and spinal fluid If such a patient does not improve after a

reasonable amount of antisyphilitic therapy the possibility of a nonspecific tumor should be suspected. Hydrocephalus, either acute or chronic, may produce symptoms closely resembling those of a brain tumor. The history and the usual absence of focal signs will help to clear up the diagnosis. If a case of multiple sclerosis begins abruptly, especially with visual changes, optic neuritis and other focal signs such as Jacksonian epilepsy, it may be misdiagnosed and operated upon for brain tumor.

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The injection of air into the ventricles is a decided help in some cases. *Encephalography* is a risky procedure in a brain tumor suspect and should under no circumstances be done if clinical and manometric signs of greatly increased pressure exist. (*See* page 1455.)

*Lumbar Puncture.*—Whether or not a lumbar puncture should be done in patients suffering from cerebral neoplasm is a disputed point. It is not as dangerous as some writers contend. If the spinal tap is done carefully, a small needle used and little fluid withdrawn, and the pressure is not elevated above 200 mm. of water, little danger will ensue to the patient. The great risk of this procedure is in tumors in the posterior fossa. Quite a few of these patients succumb suddenly due to respiratory failure. Under no circumstances should a large amount of fluid be taken out if the spinal pressure is elevated, but enough can be removed so that the important laboratory examinations on the fluid may be performed. In a patient suspected of having a tumor and without choking, an examination of the spinal fluid is indicated not only for pressure but also for syphilis.

Barany Tests.—Barany tests are of great value in localizing lesions in the cerebellopontile angle or in saying that a tumor does not exist in that region. Otherwise little help is obtained from these tests.

Electroencephalography is occasionally of help in localizing the tumor, particularly when the growth is superficially located. Recent demonstration that intracranial neoplasms tend to concentrate radioactive substances injected into the body gives promise that another helpful and valuable diagnostic technique may be developing.

*Treatment.*—The treatment of brain tumors is surgical. Brilliant results may be obtained especially when the lesion is growing from the brain coverings, although most cases do poorly. Roentgen-ray treatment is of value in a small group. The most important point in the treatment of an intracranial lesion suspected of being a tumor is to withhold operation until the diagnosis is reasonably certain.

## INJURIES OF THE BRAIN

In the analysis of a patient suffering from head injury it is important to know the following:

1. The length of the period of unconsciousness.
2. Whether paralysis or other localized cerebral symptoms existed.

3 Whether there was bleeding or escape of cerebrospinal fluid from the orifices especially the ears

4 Whether there is roentgen ray evidence of fracture of the skull

5 Was the spinal fluid bloody?

6 Were there convulsions?

A blow to the head may be followed by a fracture of the skull, injury to the brain or the meninges, cerebral blood vessels or the cranial nerves Injury to the brain may occur in the absence of definite fracture of the skull and the blow producing such injuries may be slight On the other hand many patients suffer from fracture of the skull with little or no involvement of the brain A blow producing fracture of the skull or injury to the brain may be direct or indirect and is usually followed by at least momentary loss of consciousness which may however, be very deep and lasting The commonest kind of fracture is the simple linear type depressed and comminuted ones are infrequently seen A blow on one side of the head may occasionally produce a brain injury on the opposite side (contrecoup) Fracture of the skull due to bullets or shrapnel wounds will vary according to the size of the missile and its velocity In many cases it is likely to cause more or less splintering of the bone The blow to the head with or without fracture may also produce *concussion* In many instances of concussion a simple molecular alteration in the cerebral cells occurs but it is probably true that most cases of concussion are accompanied by actual microscopic changes in the cells with secondary degeneration Numerous hemorrhages may be seen scattered through the brain of a person who has died from concussion The vessels of the brain may be torn and extensive injury and laceration of the brain may be seen A depressed fragment of bone may produce symptoms, as may also blood and the edema which follows a cerebral commotion Either or both tables of the bone may be fractured although the inner one is more usually involved Evidence of local injury to the skull may be present in the form of contusion or laceration and ecchymoses are common about the eyes and the mastoid region Those which occur in the latter area are called Battle's sign which may not appear for a number of hours Bleeding from the orifices of the head usually means fracture at the base and cerebrospinal fluid may escape as the result of such injuries In the presence of a compound or comminuted fracture or a fracture at the base of the skull with escape of blood or spinal fluid from the mouth nose or ears infection of the meninges or actual brain abscess is more likely to occur but such infection may also come on after a simpler fracture The best illustration of a simple concussion of the brain is the knock out punch given to a prize fighter the period of unconsciousness lasting but a few seconds on emerging from unconsciousness the patient may suffer from headache dizziness and vomiting The headache may be occipital frontal or generalized and is often referred to the neck

Vertigo ranks second to headache in frequency as a symptom after cerebral concussion and is often accompanied by nausea and vomiting The patient is irritable lacks concentration complains of poor memory insomnia and lack of energy and inability to work most of these symptoms being especially common in litigation cases and in those who were injured at work and strive to receive compensation It must always be remembered however that even a slight blow on the head may be followed by small hemorrhages scattered through the brain The duration of the symptoms following concussion varies greatly and one of the factors which has important bearing on the length of symptoms is the question of litigation After the acute stage has been passed headache dizziness and fatigue are commonly complained of and the importance of them is difficult to evaluate Investigation by means of the Barany tests in those cases complaining of dizziness occasionally shows evidence interpreted as being due to interference in the function of the vestibular fibers although the importance of such a finding is discounted by many Amnesia for the accident and for the events immediately preceding and following it is common

The *prognosis* in simple concussion of the brain is good one of the most important things on which to base the prognosis is the

length of the period of unconsciousness Cases may be cured only to relapse especially if legal complications occur The desire to get well is an important consideration in a head injury case

*Fracture of the skull* is accompanied by some degree of unconsciousness in practically every case, although the length of unconsciousness may vary from a few minutes to hours or days, and the patient may remain in a stupor until he dies There is usually a swelling at the site of injury and later about the eyes or mastoid region Fracture of the base is especially likely to be accompanied by injury to the cranial nerves especially the sixth seventh and eighth, a general increase of intracranial pressure will produce swelling of the optic nerves The pupils are usually unequal with a dilated pupil on the side of the cerebral injury, although they may be small and fixed to light If a hemorrhage occurs it compresses the brain or if the latter has been contused and is edematous stupor may be profound the pulse slow and the respiratory rate slow and often of the Cheyne-Stokes variety *Focal signs* will depend upon the presence of a depressed fracture collections of blood over the cortex or injury to the brain itself As the patient regains consciousness he is confused amnesic, delirious or even psychotic Korsakoff s psychosis may occur following severe injury to the brain While mental symptoms are of course frequently due to the injury a careful history of the patient s habits as regards alcohol should be obtained because in many instances the mental symptoms are more pronounced and prolonged due to the alcoholic tendencies of the individual The possibility of cerebral syphilis in one of its forms being brought out or aggravated by a head injury should also be borne in mind Not infrequently a man works successfully and intelligently up to the time of his injury from which he passes immediately into the stage of general paresis Brain tumors may be present and produce no symptoms before a head injury and afterward produce marked signs which may be confused with those due to the trauma If the fracture has gone through a sinus or if the dura has been ruptured pneumocephalus may be found on roentgen ray examination Lumbar puncture will often reveal a bloody fluid and sometimes increased pressure When the patient recovers the same symptoms that are found after a concussion are complained of but usually in a more marked degree and as in cerebral concussion, the duration of these symptoms frequently has a direct relationship to the presence or absence of litigation The *mental symptoms* that are seen after a fracture of the skull consist of loss of memory, fatigability, loss of inhibition and of attention and change in personality Mental symptoms of a hysterical nature are occasionally seen Severe injuries to the brain are followed by epilepsy in a certain percentage of cases, which has been estimated from seven to ten per cent The epileptic attacks may be localized or focal in type and while the first fit may occur during the stage of acute injury, it may be delayed a number of years Injury to the motor cortex naturally produces more instances of post traumatic epilepsy than injury to other parts of the brain but implication of parts remote from the motor cortex may be succeeded by convulsions

*Epidural hemorrhage* or *subarachnoid hemorrhages* may occur from a head trauma with or without fracture Bleeding may come on as a result of rupture of the middle meningeal artery or vein or may be due to a tearing of the sinus Just as a fracture of the skull may be produced by a blow on the opposite side so also may a traumatic hemorrhage of the brain occur on the side opposite to that to which the force was applied The frequency of epidural hemorrhage due to bleeding from the middle meningeal supply has been greatly overestimated but the importance of recognizing the syndrome producing it is extremely necessary The typical history is as follows A patient receives a blow on the head which produces momentary unconsciousness he usually though not always recovers and may even resume his work then after a short period he becomes dull stuporous and unconscious, with signs of increased intracranial pressure although the latter may be absent In fact the spinal pressure may be actually lower than normal Weakness may develop on the side opposite to the hemorrhage is progressive and is

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## PATHOLOGIC STATES OF THE NERVOUS SYSTEM OCCURRING DURING PREGNANCY AND THE PUERPERIUM

If a woman has any unusual illness during a pregnancy it is usually attributed to that condition but in many instances the neurologic condition is only coincidental. We have seen a number of brain tumors entirely unsuspected in the course of pregnancy. The symptoms resulting from these tumors, namely headache and vomiting, were thought to be due to a toxemia.

The convulsions which occur during pregnancy may be the result of toxic states induced by that condition or they may be the first manifestation of epilepsy. Hysteria may be the cause of fits during pregnancy.

Hemiplegia, an infrequent complication of pregnancy, usually occurs in the last half of the pregnancy and has been reported as occurring during the puerperium coming on one to three weeks after childbirth. The pathology of this form of hemiplegia is obscure although most of the cases are due to venous or arterial thrombosis or embolism; certainly few patients die, which would be the case if the condition were due to hemorrhage. Some of these cases may be due to a toxic factor producing encephalitis more or less limited to the motor cortex. If syphilis is present in the individual the added strain of pregnancy and delivery might readily produce thrombosis of a diseased cerebral vessel. If infection is present in a case of hemiplegia occurring during pregnancy or puerperium the possibility of an abscess or of encephalitis should be considered. Aphasia may also occur and is probably due to the same cause that produces hemiplegia.

Intracranial venous thrombrosis is a rare complication which usually appears between the fourth and the twenty first day after delivery. It is frequently characterized by headache and convulsions and is followed by monoplegia or hemiplegia with or without aphasia. Papilledema and amaurosis may occur. A third to half the patients die; those who survive may show persistent residua. Therapy is symptomatic.

The diagnosis of brain tumor in the course of pregnancy is a difficult one, and fortunately one which is not too frequently encountered. There may exist in pregnancy a type of toxemia producing choked disks, vomiting and the other signs suggestive of increased intracranial pressure. Where a doubt exists as to the presence of a brain tumor in pregnancy it is always wise to wait rather than to rush in with a surgical procedure.

Epidemic encephalitis if occurring during a pregnancy is frequently mistaken for toxemia or for a brain tumor. The choreaform type of encephalitis may be mistaken for chorea occurring during pregnancy. The most difficult differentiation is between epidemic encephalitis and toxemia. Careful and repeated laboratory examinations including that of the spinal fluid may be necessary. The occurrence of an ocular or of other cranial nerve palsies points directly toward encephalitis as the diagnosis.

Choreiform movements which occur during pregnancy may be due to chorea, encephalitis or rarely hysteria. The majority of cases appear in the first six months and are more frequent in women under the age of twenty five years. The mortality in this type of chorea has been estimated from 15 to 20 per cent.

Chorea gravidarum is likely to be more severe than Sydenham's chorea. Just as there is no mental disease peculiar to pregnancy and the puerperium it is likely that there is no chorea peculiar to these states. If hysteria and encephalitis have been ruled out, the instances of chorea are of Sydenham's type.

Peripheral multiple neuritis may complicate pregnancy or the puerperium. Such cases occurring in women who are not alcoholic are due to infections or to vitamin deficiency or to both. A psychosis may accompany the polyneuritis, as usually of the toxic type and may be of the Korsakoff variety.

Involvement of the optic nerve is usually of the toxic type secondary to kidney involvement. Real choking of the disks, however, may be seen as the result either of toxemia or of brain tumor. Disturbance of vision of various types may occur, the most

frequently accompanied by twitching or convulsions The pulse and respirations are slow, and the respirations may be of the Cheyne Stokes type Signs of pyramidal tract disease are present on the paralyzed side, although if the parietal cortex is involved, the deep reflexes may be lost Signs of meningitis are not usually present although if bleeding also occurred at the base the neck may be stiff A dilated pupil frequently exists on the side of the hemorrhage due to pressure on the third nerve by the uncus which herniates through the incisura of the tentorium

In the *diagnosis* the history is most important The treatment of the vast majority of head injuries is medical the great exception is rupture of the middle meningeal artery where prompt and efficient surgery may be lifesaving Complete rest an ice bag to the head, sedatives if the patient is restless or delirious but not in doses large enough to becloud the symptoms a continuous tub if maniacal excitement exists moderate *limitation of fluid and magnesium* sulphate by mouth or rectum is the treatment usually pursued Antibiotics should be administered to prevent the development of meningitis and pneumonia Physical restraint may be necessary

*Acute or chronic subdural hematoma* is a collection of blood between the dura and the arachnoid membranes as a rule over the convexity of the cerebral hemisphere The blow to the head responsible for the condition may be severe or extremely trivial The latent period between the receipt of the blow and the *appearance of symptoms* may vary from hours to months and according to some more than a year In some persons the lesion is bilateral In addition to trauma it may occur in such conditions as general paresis, in hemorrhagic diathesis in infections and in alcoholics but in these cases it is likely that a forgotten blow may have been the real cause of the bleeding The bleeding is originally venous and is usually small in amount The trapped blood breaks down into simpler protein molecules and by osmosis absorbs fluid from the subarachnoid space With time the hematoma enlarges and symptoms develop The inner surface of the dura is thickened either locally, or more or less extensively A combination of hemorrhage and reparative activity leads in time to marked thickening of the inner layer of the dura with adherence to the arachnoid The contents of the hemorrhagic cysts vary from a thin yellowish brown fluid to a firm clot External hydrocephalus will be pronounced The onset of *symptoms* may be apoplectiform or insidious Mental symptoms consisting of dulness irritability and delirium are common, and headache vomiting and convulsions are frequently seen The convulsions may be either focal or general Stupor, followed by pronounced coma with slow pulse and respiratory rate or Cheyne Stokes breathing may occur Signs of meningeal irritation, hemiplegia or monoplegia and papilledema are seen in some cases The hemiplegia may be present on the side of the lesion due to pressure on the opposite crus Automatic states and amnesia, disturbances of speech and of vision may be present if the hemorrhage involves other *specialized areas Fracture of the skull may* or may not be demonstrated by roentgen ray examination

The *spinal fluid* shows as a rule increased pressure may be bloody or simply xanthochromic The deep reflexes are frequently unequal usually increased but if the parietal cortex is involved they may be absent on the contralateral side Cranial nerve symptoms are usually discovered if hemorrhage has occurred at the base Dilatation of one pupil most often on the side of the hemorrhage is common There may be localized tenderness to percussion of the skull The *diagnosis* is not easy Coma may deepen or disappear in remissions The *treatment* of the condition is surgical

Both sides of the skull should be trephined because of the frequency of bilateral hematomas In any case in which the diagnosis is obscure or if the patient is supposed to have had a stroke which presents symptoms and signs that are unusual or peculiar the head should be opened this recommendation is made despite the fact that the *authors are constitutionally opposed to fishing expeditions*

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dramatic of which is sudden blindness. Occasionally retrobulbar neuritis may be seen in pregnancy. The presence of sinus disease, other sources of toxemia besides pregnancy, and hysteria should be considered. Changes in the visual fields, especially on the temporal sides, may occur in pregnancy and may be due to the enlargement of the pituitary gland. Paralysis of the motor cranial nerves is rare in pregnancy and the puerperium, but ophthalmoplegia and extra-ocular muscle palsies may occur in the polioencephalitis hemorrhagica superior of Wernicke, which sometimes accompanies hyperemesis gravidarum. This condition is due to vitamin deficiency, particularly lack of thiamin. Involvement of the spinal cord may occur at any time during pregnancy or the puerperium and may be the result of toxemia, infection, or of the severe strain of delivery. Most authorities believe that while some of the forms of myelitis or paralysis due to spinal cord disease which occur during pregnancy are secondary to such conditions as syphilis or disease of the vertebræ, the extraordinary exertion and strain incident to delivery may produce changes in the vessels of the cord. Myelitis has been known to occur in three successive pregnancies in the same woman.

## DISORDERS OF THE CENTRAL NERVOUS SYSTEM OCCURRING AT BIRTH

*Injury* to the central nervous system during birth is common and accounts for a large percentage of the deaths of babies. Blood found in the spinal fluid immediately after birth usually means injury. This does not necessarily imply that the obstetrician is in any way at fault. The usual cause is disproportion between the baby and the birth canal. Injury to the central nervous system during birth is a common cause of infantile hemiplegia, cerebral diplegia and other spastic states, the various grades of feeblemindedness and epilepsy. Though injuries to the cord are less frequently seen, they may occur in breech deliveries or in babies on whom version was practised. Another cause for injury to the brain at birth is prolonged labor with asphyxiation.

The *symptoms* of birth injury will of course depend upon the location of the injured part. The lesions most frequently involve the basal regions with the resulting symptoms of tremor, rigidity and athetosis. In these cases a diagnosis of cerebral diplegia is frequently made. If the pyramidal system has been involved on one or both sides, symptoms of such involvement will be found. A hemorrhage may occur only one one side and in such a case will produce infantile hemiplegia. The fact that the child has hemiplegia is often not recognized until it should be sitting up or walking. Convulsions are especially likely to occur in children who have had a cerebral injury. Many children who have suffered from diffuse cerebral hemorrhage without exact localizing signs are found to be late in walking and talking and show arrested cerebral development. On the other hand, a child who has had hemiplegia, the result of an injury at birth, may show little or no mental deficiency.

Implication of the spinal cord as the result of birth injury is more often due to obstetrical interference. The cord may be completely ruptured or may be the seat of partial disintegration. If the involvement is high, death as a rule results quickly. Children born prematurely may show symptoms which are confused with birth injury. The child born prematurely is a bad risk and may show signs of lack of cerebral development, and is often late in walking and talking. The pyramidal tracts are late in developing and may never develop fully. This will result in spastic paraplegia. Infection occurring in the first few weeks of life may produce inflammatory reactions in the central nervous system which are thought to be traumatic.

The *diagnosis* is difficult and much depends upon a proper history. The duration of labor, whether or not the child cried promptly after birth or gave evidence of asphyxiation, are all extremely important considerations. The occurrence of an acute infection of any description in the first few weeks of life is also important. Of equal significance is the health of the mother during pregnancy, especially whether or not she had suffered a severe infectious disease

Certain neurologic conditions occurring early in life such as hydrocephalus, microcephalus, spinal bifida various forms of muscular atrophy occurring in children and hereditary ataxia must be differentiated from birth injuries Children born after a long and difficult labor especially if instruments were used, should be subjected to careful physical examination from the neurologic standpoint In many instances a lumbar puncture may be necessary to aid in the diagnosis

If an intracerebral hemorrhage exists it must be *treated* accordingly If however, blood is found in the spinal fluid and the examination does not indicate that the hemorrhage has occurred into the brain the patient should be treated as one of subarachnoid bleeding Decompressive operations should be resorted to only as a last resort and will usually be unavailing If, however signs exist pointing to a localized hemorrhage surgery should be given a chance Occasionally a baby who has an extracerebral hematoma will develop enlargement of head simulating hydrocephalus operation is indicated in such cases If the child survives to the age of three or four years or beyond he will often be found to be a case for speech training and frequently will have to be sent to a special school depending upon the amount of intellectual damage done If infantile hemiplegia results various orthopedic operations may assist the child in making the greatest use of the power which exists but is unavailable because of contractures On the other hand patients are subjected to operation without beneficial result While carefully considered physiotherapeutic exercises and orthopedic operations may be of value in enabling the child with cerebral palsy to make the best use of such functioning muscle power as he has it must be borne in mind that no amount of retraining or surgery will restore the damaged neural tissues

### Internal Hydrocephalus

Internal hydrocephalus is a condition in which there is an increase in the amount of fluid within the ventricles of the brain with consequent enlargement of the ventricles The total amount of fluid under normal conditions varies from 100 to 200 cc An unusual rate of production or an interference with the outward flow leads to hydrocephalus The usual cause of this condition is a block somewhere along the closed system in which the fluid circulates but it may also be due to an excessive production or inadequate absorption of the spinal fluid The usual location of the block is in the region of the fourth ventricle In this case all of the ventricles are enlarged If the escape of the fluid is interfered with at the arachnoid villi there is free circulation through the ventricles, but the fluid cannot be absorbed through the sinuses This produces both internal and external hydrocephalus The cause of internal hydrocephalus which is the common variety may be a congenital anomaly tumor infection or injury The common infection is meningitis, which causes adhesions around the foramina of Magendie and Luschka and prevents the escape of fluid from these orifices In such cases it is difficult to obtain much spinal fluid by lumbar puncture Tumors in the posterior fossa frequently produce internal hydrocephalus as may also tumors in or close to the ventricular system Injuries producing bleeding in the subarachnoid space particularly at birth may lead to adhesions and the formation of an obstructive type of hydrocephalus Congenital syphilis tuberculous parentage rickets and heredity at times play a role in the production of hydrocephalus

The *symptoms* of hydrocephalus are usually present in some degree at birth which may be difficult or impossible because of the size of the head The circumference of the head normally is 35 to 40 cm at birth may be increased two or three times in hydrocephalus The skull is round the frontal end is prominent the sutures are separated and the fontanels are wide and often pulsate The scalp is thin and the patient has little or no hair The face in contrast to the skull seems small and triangular The scleræ are visible and the eyes are widely separated The child is a poor specimen physically may be hemiplegic or paraplegic and if it learns to walk at all it does so late Convulsions and optic atrophy are common Various grades of

*retarded mentality are found* from the rare case which is almost normal to low grade idiots These patients are extremely susceptible to infections, and as a rule die early in life Hydrocephalus is often associated with other peculiarities of development, such as spinal bifida or encephalocele

The *diagnosis* should offer little difficulty The injection of dyes may be used to determine whether the hydrocephalus is communicating or obstructive The dye is injected into one of the lateral ventricles If the hydrocephalus is of the communicating type, it will be recovered by the lumbar puncture If there is no recovery of the fluid from the lumbar tap, there is an obstruction somewhere in the ventricular system Encephalography or ventriculography may be used to obtain a detailed picture If hydrocephalus occurs after the sutures are closed signs of increased intracranial pressure ensue These cases are practically always due to *meningitis or tumor although* rarely fracture of the base with subarachnoid bleeding may block the escape of fluid

The *treatment* of hydrocephalus usually produces no satisfactory results Although a few good results have been reported by surgical procedures in which new openings are made for the escape of fluid such as that from the third ventricle into the underlying cistern or cauterization of the choroid *most of the procedures recommended are* palliative If syphilis is present antiluetic treatment should be pushed

### Infantile Hemiplegia

As a result of trauma or asphyxiation during birth or due to encephalitis the result of infections of practically any variety or to an embolism an infant may become hemiplegic This will make the child slow in walking and talking and a candidate for epilepsy If the hemiplegia is on the right side, speech if present may be lost but may be regained or reappear probably by the training of the centers on the opposite side of the brain If the hemiplegia is produced by encephalitis occurring in the cortex Jacksonian epilepsy or partial continuous epilepsy may be present If hemiplegia develops in an infant the limbs on the paralyzed side do not develop and are smaller and shorter than *their fellows and there* is a marked tendency toward contractures at the wrist fingers and ankle In this type of case orthopedic operations may do considerable good although these procedures are certainly not underdone

### Little s Disease

In infants born prematurely and sometimes in twins the pyramidal tracts fail to develop properly As a result spastic paraplegia with signs of pyramidal tract disease exists The upper extremities may be involved but not to the extent of the lower In other cases the upper extremities escape entirely and the mentality of the child may be normal In some instances there is a general arrest of cerebral development the mentality of the child is greatly affected and the speech may be restricted or absent Convulsions occasionally occur While children suffering from this condition are late in walking they may develop a fair gait

The causes of the various types of paralysis that occur in infants are somewhat beclouded The factors at fault are defective genes premature birth difficult and prolonged labor especially instrumental ones and asphyxiation Acute infectious disease of the mother during pregnancy may account for changes in the central nervous system of the fetus and acute infections of the child in the first few weeks of life may produce encephalitis which subsequently leads to various types of paralysis Convulsions occurring early in life may be followed by a cerebral hemorrhage *Epilepsy various grades of mental retardation* speech defects ocular palsies and irregular movements especially athetosis are common complications Occasionally the cerebellum seems to be particularly involved

### Tay-Sachs Disease

Amaurotic family idiocy (Tay-Sachs disease) is a combination of blindness from optic atrophy and idiocy from arrested cerebral development A child who appears normal at birth shows the foregoing symptoms usually in the first year of *life It is particularly common* in Polish Jewish children The condition is often familial Gradual signs of cerebral diplegia occur with nystagmus and diminution of vision followed by blindness The course of the condition is rapid the child usually dying before the age of six years One of the most characteristic signs in the examination of the patient is a cherry red spot seen at the macula This is due to atrophy of the retina which permits the choroid to shine through

## BULBAR AND PSEUDOBULBAR PALSY

### Bulbar Palsy

This condition is frequently a part of the picture of amyotrophic lateral sclerosis progressive spinal muscular atrophy acute anterior poliomyelitis and may be the first symptom of these conditons It comes on as a rule during or after the fifth decade in nonpoliomyelitic cases The pathologic changes consist of degeneration of the lower nuclei of the seventh the ninth, tenth and twelfth cranial nerves The upper parts of the seventh nerve nuclei occasionally and at times the motor fifth are implicated The *symptoms* are difficulty in speaking swallowing chewing and phonation coming on gradually The speech develops a nasal twang The labials and linguals are pronounced with difficulty and the speech gradually becomes worse and worse so that in time anarthria results The same thing takes place as far as swallowing is concerned so that in time food may regurgitate through the nose or lodge in the larynx A progressive atrophy occurs in the muscles of the lips tongue larynx and also in those of mastication All the signs of anterior horn disease occur in the atrophic muscles

The *diagnosis* is to be made from pseudo bulbar palsy encephalitis or myasthenia gravis which is in reality bulbar palsy without anatomic findings Tumors of the bulb must also be differentiated

There is no successful *treatment* and the patient usually succumbs within two years of the onset

### Pseudobulbar Palsy

Strictly speaking this is not a disease but a syndrome depending upon bilateral cerebral lesions involving the upper motor neurons These lesions are usually the result of vascular disease with encephalomalacia Any one of the numerous processes which may produce bilateral lesions in the brain may be the etiologic fault thus arteriosclerosis syphilis chronic encephalitis multiple sclerosis and multiple emboli may be the cause of pseudobulbar palsy



The movements which are controlled bilaterally from the cortex are not markedly involved by a unilateral lesion thus in the ordinary type of hemiplegia swallowing and chewing are little affected and usually only early in the illness In bilateral lesions, however these functions are interfered with In a pseudobulbar palsy the lesions are above the nuclei and the symptoms of anterior horn disease seen in bulbar palsy are lacking In pseudobulbar palsy the patient has a spastic involvement of the muscles supplied by the bulb

The history of the onset is most important It is discovered that the patient has had at least two apoplectic attacks one involving each side of the body and it is frequently true that one of the attacks was mild In some of the patients the hemiplegia lasts only a short time After bilateral lesions have occurred the patient develops difficulty in chewing, swallowing and talking Difficulty in chewing and swallowing may be so pronounced that the patient has trouble obtaining enough nourishment He frequently chokes and food may regurgitate through the nose The difficulty in speech may vary from a mild dysarthria to anarthria Attacks of involuntary emotionalism are common and the patient may have uncontrollable laughter or crying without cause Anything which plays upon the emotions of the individual may serve to bring further involuntary laughter or crying especially is this so of the latter

Signs of pyramidal tract disease may be present on both sides of the body and the gait may be characteristic of cerebrospinal arteriosclerosis namely the gait of little steps it may be spastic on one or both sides In pseudobulbar palsy one may also see *symptoms* referable to any part of the brain These symptoms will of course depend upon the location of the pathologic lesions Disturbance in the control of the sphincters may also be present

The *diagnosis* of pseudobulbar palsy is usually easy and is made on the history the involuntary emotionalism difficulty in chewing and swallowing and talking without the signs of nuclear disease Occasionally pseudobulbar palsy with attacks of involun-

retarded mentality are found, from the rare case which is almost normal to low grade idiots These patients are extremely susceptible to infections and as a rule die early in life Hydrocephalus is often associated with other peculiarities of development, such as spinal bifida or encephalocele

The *diagnosis* should offer little difficulty The injection of dyes may be used to determine whether the hydrocephalus is communicating or obstructive The dye is injected into one of the lateral ventricles If the hydrocephalus is of the communicating type it will be recovered by the lumbar puncture If there is no recovery of the fluid from the lumbar tap there is an obstruction somewhere in the ventricular system Encephalography or ventriculography may be used to obtain a detailed picture If hydrocephalus occurs after the sutures are closed signs of increased intracranial pressure ensue These cases are practically always *due to meningitis or tumor although* rarely fracture of the base with subarachnoid bleeding may block the escape of fluid

The *treatment* of hydrocephalus usually produces no satisfactory results Although a few good results have been reported by surgical procedures in which new openings are made for the escape of fluid such as that from the third ventricle into the underlying cistern or cauterization of the choroid most of the procedures recommended are palliative If syphilis is present antiluetic treatment should be pushed

### Infantile Hemiplegia

As a result of trauma or asphyxiation during birth or due to encephalitis the result of infections of practically any variety or to an embolism an infant may become hemiplegic This will make the child slow in walking and talking and a candidate for epilepsy If the hemiplegia is on the right side speech if present may be lost but may be regained or reappear probably by the training of the centers on the opposite side of the brain If the hemiplegia is produced by encephalitis occurring in the cortex Jacksonian epilepsy or partial continuous epilepsy may be present If hemiplegia develops in an infant the limbs on the paralyzed side do not develop and are smaller and shorter than their fellows and there is a marked tendency toward contractures at the wrist, fingers and ankle In this type of case orthopedic operations may do considerable good although these procedures are certainly not underdone

### Little s Disease

In infants born prematurely and sometimes in twins the pyramidal tracts fail to develop properly As a result spastic paraplegia with signs of pyramidal tract disease exists The upper extremities may be involved but not to the extent of the lower In other cases the upper extremities escape entirely and the mentality of the child may be normal In some instances there is a general arrest of cerebral development the mentality of the child is greatly affected and the speech may be restricted or absent Convulsions occasionally occur While children suffering from this *condition are late in walking they may develop* a fair gait

The causes of the various types of paralysis that occur in infants are somewhat beclouded The factors at fault are defective genes premature birth difficult and prolonged labor especially instrumental ones and asphyxiation Acute infectious disease of the mother during pregnancy may account for changes in the central nervous system of the fetus and acute infections of the child in the first few weeks of life may produce encephalitis which subsequently leads to various types of paralysis Convulsions occurring early in life may be followed by a cerebral hemorrhage Epilepsy various grades of mental retardation speech defect ocular palsies and irregular movements especially athetosis are common complications Occasionally the cerebellum seems to be particularly involved

### Tay Sachs Disease

Amaurotic family idiocy (Tay Sachs disease) is a combination of blindness from optic atrophy and idiocy from arrested cerebral development A child who appears normal at birth shows the foregoing symptoms usually in the first year of life It is particularly common in Polish Jewish children The condition is often familial Gradual signs of cerebral diplegia occur with nystagmus and diminution of vision followed by blindness The course of the condition is rapid the child usually dying before the age of six years *One of* the most characteristic signs in the examination of the patient is a cherry red spot seen at the macula This is due to atrophy of the retina which permits the choroid to shine through

lethargy, and clouding of consciousness. In addition there are varying degrees of ophthalmoplegia, ataxia and tremor. There may be an associated peripheral neuropathy. In untreated cases the course is rapidly progressive, stupor deepens and death ensues. Large doses of thiamin and other vitamins produce improvement particularly of the *ophthalmoplegia*, but many of the recovered cases show a Korsakoff's psychosis.

## DISEASES DUE TO DISORDERS OF THE EXTRAPYRAMIDAL MOTOR SYSTEM

### PARALYSIS AGITANS

*Synonyms.*—Parkinson's disease. Shaking palsy.

*Definition.*—Paralysis agitans is a chronic, slowly progressive disorder characterized by tremor and rigidity and due to changes in the extrapyramidal motor system.

A definite *etiologic factor* has never been found, although the Parkinsonian syndrome is extremely common after epidemic encephalitis and is due in such cases to inflammatory changes. It may be that many of the cases that we consider ordinary paralysis agitans are in reality due to infections which caused encephalitis years before the onset of the symptoms of paralysis agitans. This is particularly true in the juvenile types of the disease. Others are of the opinion that the disease is primarily a degenerative disorder not unlike that occurring in the cerebral cortex in senile dementia. Although hereditary and familial forms have been reported, they are extremely uncommon. Men are affected much more frequently than women and the disease usually appears after the age of forty five years. Emotions and injuries have been mentioned as etiologic factors. In the latter case it is likely small hemorrhages occur in the basal ganglia. Syphilis probably plays very little if any role in the production of paralysis agitans. Large tumors in the frontal areas of the brain may very rarely produce Parkinsonism.

*Symptoms.*—These appear insidiously and little change may take place for weeks or months. In the early stage of the disease the tremor, which is usually the first symptom to be noticed, may disappear for a short time. The tremor as a rule first appears in an upper extremity and practically always in the hand or fingers. It is rhythmical, may be either fine or coarse and vibrations range from four to seven a second. In the early stages it may be limited to one finger or thumb, then gradually spreads to involve the entire upper extremity, the lower extremity of the same side and then usually involves the other side of the body. It may, however, remain unilateral for a number of months or longer. The tremor is present during rest and ceases or diminishes during an action. An occasional patient can control the tremor voluntarily but in such a case, as in a tic, the tremor may then be exaggerated temporarily. The characteristic tremor is the pill rolling one, but flexion and extension of the wrist and fingers or pronation and supination of the forearm are common without a definite pill rolling element. The tremor may involve the head, jaw and occasionally the tongue. Like practically all irregular movements it disappears during sleep. The tremor may be imparted to the handwriting and the tremor plus rigidity produce a progressive smallness of the handwriting which is characteristic of the disease.

*Objective Signs.*—Although there are types of paralysis agitans in which rigidity is marked and the tremor slight or absent (the so-called *paralysis agitans sine agitatione*) the rigidity usually follows the tremor. When the extremities are passively moved a wax like resistance occurs, the cogwheel symptom. Rigidity of the face causes the masked expression, the bodily attitude is that of the position of an old bent man, the trunk flexed, head flexed and slight flexion of the upper extremities and at the knees. The hand may assume various positions, the flipper hand being not uncommon. The thumb may be held in the palm of the hand and the fingers flexed over it. Because of the rigidity all voluntary movement is slowly initiated and slowly carried out. A common sign early in the disease is the inability to approximate and separate rapidly the thumb and forefinger on at least one side. Change

tary weeping is mistaken for manic depressive insanity in the depressed phase

The *outlook* in cases of pseudobulbar palsy is poor Some of these patients choke to death or develop pneumonia due to the difficulty in swallowing so that special care is necessary as far as feeding is concerned

### Myasthenia Gravis

*Asthenic bulbar paralysis* also referred to as *bulbar palsy without anatomic findings* is a relatively uncommon disease of the muscular system and is without definite neuropathologic changes The endocrine system may be at fault In many cases an enlarged persistent thymus or a lymphoid tumor of the thymus gland has been found at necropsy The muscles most frequently affected are those of the eyes face and tongue, throat and neck although all the muscles of the body may be involved and sudden death probably from involvement of the myocardium has been reported The muscles may be infiltrated with round cells Recent studies indicate that myasthenia is primarily a disorder of the myoneural junction Ordinarily the transmission of nerve impulses at the myoneural junction depends on the liberation of acetylcholine In myasthenia there is either a deficient liberation of acetylcholine or else acetylcholine is rapidly destroyed by cholinesterase Prostigmine inhibits cholinesterase activity while quinine increases it

The most important *symptom* of myasthenia gravis is weakness or paralysis of the muscles brought on by use and relieved by rest As mentioned before the muscles most usually affected are those of the eyes resulting in ptosis and diplopia of the lips tongue, pharynx and jaw resulting in dysarthria dysphagia and difficulty in chewing and of the muscles of the neck resulting in difficulty in holding the head erect In occasional cases the muscles of the trunk and extremities may also be involved To elicit the symptoms it is only necessary to have the patient perform some given muscular effort a number of times When the muscles become fatigued movement is no longer possible The same thing in a way is accomplished by stimulating the muscles with faradic current After a number of stimulations the muscle reacts feebly and finally fails to respond, after a rest the excitability returns (Jolly reaction) The disease is more frequently seen between the ages of twenty and fifty years females are more often involved than males Remissions are common Sensory loss atrophy fibrillations and the reversal of the electrical reactions do not occur Remissions often occur during pregnancy The outlook is bad for recovery

The *diagnosis* is to be made from bulbar palsy encephalitis hysteria tumors of the bulb cerebral syphilis and tumors of the corpora quadrigemina There is no entirely successful *treatment* of the disease The patient should be placed at rest and fatigue avoided The diet should be soft and liquid Tonics ephedrine sulphate and pilocarpine and epinephrine *are* recommended Prostigmine has given valuable aid both in the diagnosis and treatment of the disease An injection of the drug causes a rapid and usually complete disappearance of the symptoms whereas other conditions do not respond The drug should be used hypodermically for quick results and as a therapeutic test Prostigmine can also be given by mouth 15 mg every two to four hours The dosage must be individualized In many patients after prolonged administration the drug becomes progressively less effective Ephedrine augments the effect of prostigmine There have been reports of improvement following thymectomy especially when a thymic tumor is found

### WERNICKE S POLIOENCEPHALITIS

Polioencephalitis hemorrhagica superior of Wernicke occurs in association with chronic alcoholism hyperemesis gravidarum gastric carcinoma and other conditions in which there may be a disturbance of nutrition The disease is probably due to vitamin deficiency particularly of thiamin The pathologic changes consist of petechial hemorrhages vascular proliferation and mild nerve cell damage in the periaqueductal region the mammillary bodies the walls of the third ventricle and the gray matter of the floor of the fourth ventricle Clinically it is characterized by headache, dizziness vomiting

comes in contact should be agreeable kindly and optimistic He should avoid excitement and excessive physical exertion Hydrotherapy mild massage passive movement and exercises within reason are indicated Sometimes mild electricity seems to improve the sufferer from paralysis agitans largely because of its psychic effect From the drug standpoint a combination of bromide and hyoscine does most to relieve the tremor The dose of these drugs should be small at first and gradually increased In some cases tincture of stramonium has a beneficial effect upon the tremor New drugs such as artane, panparnit tolserol and benadryl have recently been introduced but so far have produced no dramatic beneficial results Sleeplessness pain and distress in the extremities caused by tremor and rigidity call for the use of hypnotics and analgesics In the patient with advanced paralysis agitans who suffers intensely it is as justifiable to prescribe opium in some form as it is to do so for cancer The use of such drugs as tobacco coffee tea and alcohol are capable of producing tremor and should be forbidden Phenobarbital and allied drugs make the patient worse Dexedrine and Benzedrine apparently has a beneficial effect in respect to relief of tension and relieving the depressive symptoms

Various operative procedures such as cutting the pyramidal tracts and ablation of the premotor cortex have been advocated In our experience they have produced no good results and at present must be regarded as experimental

## SYDENHAM S CHOREA

*Synonyms* —St Vitus dance Acute chorea

For years Sydenham s chorea was thought to be a functional nervous disorder but it is now *considered* an infectious disease closely allied to rheumatic fever It has no relation to epidemic encephalitis which however has a choreiform type A mental shock or trauma sometimes seems to bring on the disease certainly they exaggerate the condition if already present The disease has a tendency to be complicated by endocarditis polyarthritis and tonsillitis The pathology of Sydenham s chorea is not on a firm basis although it is assumed that changes in the corpus striatum are responsible for the choreiform movements The brain may be hyperemic and occasionally if a case is complicated by endocarditis emboli may occur Eosinophilia is frequently found

The disease is one which occurs particularly between the ages of five and fifteen years, and girls are more susceptible than boys The disease is *more frequent* in February and March and in October and November Heredity has nothing to do with the onset of the acute chorea and hereditary chorea and Sydenham s chorea have no relation as far as etiology is concerned It is more common in races which are temperamental, and also is seen more frequently in children who are in a low state *of general health Pregnancy predisposes to Sydenham s chorea* and relapses of chorea are especially common during pregnancy The first pregnancy is more likely to be complicated by chorea than later ones

*Symptoms* —The disease usually appears gradually The child is out of sorts and suffers from headache anorexia and a general slowing up The temperature may be slightly *elevated during the early* stages of chorea The choreiform movements may be localized to one side of the body or to one extremity or they may be generalized The movements are slow and purposeless never rhythmical and as far as rapidity is concerned are midway between athetosis and tic Like practically all spontaneous movements they cease during sleep *though in some cases they may be so* severe as to prevent sleep Any movement which the patient attempts will be affected if the part used is choreic Throughout the disease for example the patient suffering with acute chorea has difficulty in feeding himself and frequently drops dishes The child has a tendency in performing an act to overdo it At first one side may be affected more than the other and in rare cases chorea may be confined to one side but as a rule both sides of the body are irregularly affected as the disease progresses Involvement of the muscles of speech is common and in severe cases the speech is extremely dysarthric When the choreiform

of position is difficult and often impossible The common maneuver in getting up is for the nurse to grasp both hands of the patient and slowly pull him to a standing position A common complaint in patients with paralysis agitans is their inability to turn over in bed many of them if they desire to change their position must get out of bed and then re-enter it The winking reflex is usually affected An involuntary step backward or to either side as the patient arises from a sitting position is a common symptom and may be among the earliest These signs are referred to as retropulsion and lateropulsion The most characteristic thing as the patient walks is the loss of the automatic swinging movements of the arms the foot drags and shuffles Another characteristic of the gait usually not seen until the disease has advanced is *festination* In this condition the patient starts off slowly and then the rate of progression becomes more rapid until he is running and the body is bent forward Although it would seem as though he must fall he rarely does so He stops himself by grasping hold of a person or an object in his path

The various emotions are rarely transmitted to the facial expression although a wan ghost like smile occasionally occurs Anger or displeasure may cause flushing of the face The loss of movement which occurs is not a paralysis in the ordinary sense of the word but is more an inhibition of motion due to rigidity which may become so pronounced that the patient has practically no voluntary movement left except in the eyes Reflex acts such as swallowing are not affected if at all until late in the disease and the sphincters usually remain intact Speech often a monotone may develop a sort of festination and as the disease progresses the patient may become completely anarthric The deep reflexes are normal or slightly hyperactive but if much rigidity is present they may be difficult to obtain The superficial reflexes are normal Babinski s sign does not occur in the ordinary case of paralysis agitans

Sensation objectively tested is not involved Pain is not an infrequent symptom in paralysis agitans, especially in the upper extremities It is probably due to the muscular rigidity and pull on the joints A burning sensation is not uncommon and flushing and excessive sweating are frequently seen Patients with paralysis agitans often stand the cold much better than the hot weather and some of them are much better when they wear light clothing Salivation a common symptom in the Parkinsonism due to epidemic encephalitis is not so frequently seen in the ordinary type of the disease The mentality of patients suffering from paralysis agitans is not altered although they are often fussy irritable and unreasonable They are more subject to depression than the normal person, and also more likely to develop a real psychosis which is usually of a depressive suspicious nature

*Diagnosis* —In the early stage of the disease when the tremor is slight neuralgic pains present and nothing found to account for them the patient suffering from Parkinsonism may be thought to be psychoneurotic The tremor of paralysis agitans will disappear on the paralyzed side if the patient has an attack of cerebral thrombosis The tremor of senility will probably offer the greatest difficulty in differentiation This tremor affects chiefly the head and upper extremities and is increased during action The so-called rabbit tremor or jaw tremor is more characteristic in the senile case Multiple sclerosis and other forms of irregular movement such as chorea and athetosis should not be difficult to differentiate It is often difficult to say whether a patient suffering from paralysis agitans is a victim of the degenerative type of the disease or whether he has Parkinsonism due to chronic encephalitis The distinction will be particularly difficult in those cases of chronic encephalitis where there is no history of an acute infection

The *prognosis* in paralysis agitans is unfavorable for recovery The outlook for life is good the patient often living from five to twenty years The duration depends largely upon the age of onset

*Treatment* —No known treatment is curative however much can be done to help the patient and to relieve his suffering He should be placed in the best possible state of general health he should have pleasant surroundings and the people with whom he

comes in contact should be agreeable kindly and optimistic He should avoid excitement and excessive physical exertion Hydrotherapy mild massage passive movement and exercises within reason are indicated Sometimes mild electricity seems to improve the sufferer from paralysis agitans largely *because of its psychic effect From the drug* standpoint a combination of bromide and hyoscine does most to relieve the tremor The dose of these drugs should be small at first and gradually increased In some cases tincture of stramonium has a beneficial effect upon the tremor New drugs such as artane, panparnit tolserol and benadryl have recently been introduced but so far have produced no dramatic beneficial results Sleeplessness pain and distress in the extremities caused by tremor and rigidity call for the use of hypnotics and analgesics *In the patient with advanced paralysis* agitans who suffers intensely it is as justifiable to prescribe opium in some form as it is to do so for cancer The use of such drugs as tobacco coffee tea and alcohol are capable of producing tremor and should be forbidden Phenobarbital and allied drugs make the patient worse Dexedrine and Benzedrine apparently has a beneficial effect in respect to relief of tension and relieving the depressive symptoms

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movements affect the face *grimacing* results and involvement of the tongue produces disturbance of speech and chewing. Due to the irregular movements and the incoordination which results, weakness of the *affected* extremities may be present and may be so pronounced as to produce the so called paralytic type of the disease. While pyramidal tract signs may be seen they certainly are extremely rare. It is quite common in any form of chorea for the great toe to extend as a manifestation of chorea *if the plantar surface is stimulated just as this* choreiform movement occurs, the patient may be thought to have a Babinski sign. Inasmuch as the state of the deep reflexes varies there is nothing characteristic about *them*. Excitement and fatigue increase the movements. The pupils and ocular nerves electrical reactions and sensation are normal. Pain may occur in the extremities especially if the movements are severe or if the individual has arthritis. The patient suffering from Sydenham's chorea is irritable dull and shows a general *reduction in his mental* faculties. A toxic exhaustive psychosis may ensue, with excitement visual and auditory hallucinations and delusions. Cases of chorea complicating pregnancy are especially liable to develop *mental symptoms* (chorea insaniens). Evidence of tonsillitis arthritis and endocarditis may be found. The average duration of Sydenham's chorea is two or three months the extremes being six weeks to eight months. *Occasionally a more* or less chronic state may ensue.

The greatest mistake in *diagnosis* is in calling cases of tic or habit spasm chorea. The tic or habit spasm is quick apparently purposeful usually limited to certain groups of muscles and does not vary from week to week. They are especially likely to involve the face head or shoulders. Choreiform and choreo athetoid movements may occur in the acute stage of epidemic encephalitis or may be a manifestation of chronic encephalitis. The *movements* appear much more rapidly in encephalitis as a rule they are more marked and are accompanied by other signs especially ocular palsies. *Hysteria may be* mistaken for chorea especially in pregnancy. The irregular *movements* which occur in hysteria are usually not distinctly chorei form but are more tic like in character. Furthermore, the patient usually responds quickly to isolation and *psychotherapy*.

The *prognosis* for recovery is excellent, an occasional patient dies but rarely does the disease become chronic. The death rate in chorea complicated by pregnancy has been *estimated as high as 20 per cent, but this* figure is probably too high. If endocarditis occurs signs of that affection will persist.

*Treatment*.—The most important consideration is rest in bed which should be continued until the movements have disappeared. The patient should be placed in the sunniest and best ventilated room in the house and visitors excluded. Stimulating games and reading should not be permitted. In view of the fact that many of the children are underweight and undernourished a *high caloric high vitamin diet rich in greens* and fruit should be ordered. Hydrotherapy, especially a continuous warm tub if available decreases the choreiform movements as do also warm packs or an ordinary warm bath. *The drugs found most efficacious are* bromides and salicylates. Barbituric preparations may be used for their hypnotic and sedative effects. Nonspecific protein therapy such as typhoid vaccine and the in*duction of fever by the hypertherm have* been recommended. The writers have seen excellent results in which the course of the disease was cut short by short courses of fever therapy. Particular attention should *be paid to the general health of the patient* he should be given plenty of fresh air and sunshine bad teeth and tonsils should be removed and other infections such as pyelitis cleared up. If endocarditis has occurred *the child should be kept in bed for a longer* period of time. After the movements have ceased the child may be gotten out of bed by easy stages permitting him to go downstairs and then out of the house. It will *usually not be necessary to employ physiotherapy* although occasionally massage may be beneficial. Stimulating physiotherapeutic treatment such as electricity should not be used.

## HUNTINGTON'S CHOREA

Hereditary chorea begins about the age of thirty five or forty years usually involves

more than one member of a family and the history of its occurrence in the family may date back many years On the other hand occasional cases of Huntington's chorea are seen in which the family occurrence of the disease is absent The main facts on which the diagnosis is based are heredity choreiform movements and dementia The choreiform movement as a rule begins in one hand or in the face and then gradually spreads to involve the entire body The irregular movements do not differ from those of Sydenham's chorea When the disease is far advanced it is necessary to confine the patient to a wheel chair or bed because the violence of the movements causes falls and injuries Movements of the face produce *grimacing and those of the trunk pelvis* and lower extremities produce a bizarre disordered gait the patient dipping and swaying forward backward and to either side Mentally the patient deteriorates and if he lives long enough suffers from complete dementia

In the early stages he may show ideas of persecution and get into legal difficulties because of poor judgment and loss of memory As in most hereditary diseases males are affected more than females In a family in which this disease exists there may be instances of chorea without dementia mental disease without chorea and some *instances in which neither distinct mental* disease nor chorea is found but some members of the *family however are queer* and eccentric

Huntington's chorea has no relation to Sydenham's chorea and rheumatic infections The underlying *pathology* of Huntington's chorea is an atrophy of the motor cells of the corpus striatum and also atrophy of the frontal cortex At times changes suggestive of encephalitis are found in the brain The disease is progressive incurable and may last from one to fifteen years or more *Huntington's chorea may be confused with* other forms of chorea produced by changes in the basal ganglia

The *treatment* is ineffectual but for a time the chorea may be controlled by sedatives such as bromide hyoscine and stramonium It is practically always necessary with time to institutionalize the patient Marriage of members of families in which the disease exists should be discouraged

## PROGRESSIVE LENTICULAR DEGENERATION

A description of progressive lenticular degeneration by Wilson in 1912 focused attention on the basal ganglia Wilson's disease is a familial condition appearing as a rule before the age of thirty years and complicated by a hob-nail cirrhosis of the liver It is characterized by a rhythmic tremor of the extremities sometimes of the paralysis agitans type although occasionally *choreiform or athetoid movements are seen* The tremor unlike that of paralysis agitans *is increased by action The extremities* and face are hypertonic the hypertonicity of the muscles of the face producing a spastic smile Involuntary emotionalism especially of laughter is commonly seen Because of the hypertonicity of the extremities contractures develop The deep reflexes are usually hyperactive but positive signs of pyramidal tract disease are lacking True paralysis is not present but the scope of movement is greatly limited because of tremor and rigidity The pupils cranial nerves abdominal reflexes and sensation are normal The involvement of the muscles of speech and swallowing produce dysarthria *and dysphagia The disease is progressive* incurable and fatal as a rule under ten years

In addition to hob-nail cirrhosis of the liver *postmortem examination* reveals degeneration of the lenticular nuclei most marked in the putamen and to a less degree in the globus pallidus The degeneration sometimes ends in cavitation

### PSEUDOSCLEROSIS

The syndrome of pseudosclerosis is similar *in many respects* to Wilson's disease and by many Wilson's disease and pseudosclerosis are considered *varieties of the same* condition Cirrhosis of the liver is found in both although more frequently in Wilson's disease Enlargement of the spleen is sometimes found in pseudosclerosis Tremor especially an intention tremor is commonly

seen in pseudosclerosis and rigidity is usually absent In pseudosclerosis a peculiar greenish discoloration of the corneal margins is frequently observed This has been called the Kayser-Fleischer ring or Fleischer-Strumpell ring The speech and type of tremor may suggest multiple sclerosis but nystagmus optic atrophy, *pyramidal tract signs and* alteration of the colloidal gold curve test are absent

## EPIDEMIC ENCEPHALITIS

The condition which we now commonly refer to as epidemic encephalitis was first described by von Economo under the title of *lethargic encephalitis* There is much in medical history to indicate that the disease has been prevalent in the past and has been described under various titles After its appearance in Europe, in 1917, the disease spread over the entire world The first cases in the United States occurred toward the end of 1918 and the early part of 1919 The first great epidemic of encephalitis came after the severe and widespread epidemic of influenza The type of the disease varied in *different years* It is not contagious in the ordinary sense of the word and while more than one case has occurred in a family even this is *uncommon The writers have never* seen a case develop in a hospital ward either among other patients or among the doctors and *nurses handling cases of epi*demic encephalitis

*Pathogenesis* —The cause of the disease is supposed to be a *filtrable virus Whether* there is a relation between encephalitis and influenza or encephalitis and poliomyelitis and epidemic meningitis is not known There is much evidence to associate herpes febrilis and encephalitis and also perhaps chickenpox The infection probably enters through the naso pharynx and the incubation period is about ten days

*Pathology* —The brunt of the disease is borne by the region of the aqueduct of Sylvius, the basal ganglia the pons and medulla and substantia nigra While the cortex and spinal cord may be involved the disease has a predilection for the parts mentioned The meninges usually show a mild to moderate inflammatory reaction

*Microscopically* the chief feature is a perivascular infiltration with lymph or round cells In the subacute and chronic cases of encephalitis changes are found, especially in the *corpus striatum thalamus, in the* hypothalamic structures and in the substantia nigra Changes in other parts of the *nervous system may* be discovered, but are uncommon The vessel walls often show degeneration and pseudocalcareous deposits

*Symptoms* —The disease involves the sexes about equally and, while it occurs at any age, young adults are more frequently involved Many types of the disease have been described as far as symptomatology is concerned, and the various types mean nothing more nor less than that different parts of the nervous system are affected by the virus The symptomatology varies in different years The most common symptoms are headache, lethargy and diplopia The temperature is elevated as a rule, but does not often go above 101° to 102° F The lethargy varies from a slight stupor to a profound coma Quite often even in the deepest stupor the patient may be aroused He will then carry out a command or two and *drop back to sleep The ocular palsies* present in the disease are due to the inflammatory reactions in or near the nuclei of *these nerves The ocular palsies* either persist or clear up and other cranial nuclei may be involved especially the seventh *Therefore a bilateral facial palsy giving an* expressionless appearance to the face is seen An acute bulbar palsy is occasionally a manifestation of *epidemic encephalitis There* is no other disease which produces an irregular succession of cranial nerve paralyses in the course of a few hours or a few days and quite often as a fresh involvement occurs the nerves first involved clear up Nuchal rigidity and Kernig s sign are frequently seen in the acute stage of epidemic encephalitis and in the first two or three years in which the disease became *prevalent* often led to the erroneous diagnosis of meningitis especially tuberculous Involvement of the *bulb produces dangerous* symptoms often with irregularity of the pulse and respiration and is a common cause of death which may *occur suddenly* Catatonia occasionally is seen This symptom may

lead to mistakes in diagnosis such as hysteria or dementia precox The deep reflexes are frequently unaltered, and Babinski s sign a great rarity *Involvement of the sphincters* does not usually occur but incontinence of urine is occasionally seen probably due to the stupor of the patient Impairment of *accommodation and loss of pupillary re*action are frequently seen in the acute stage A paralysis agitans syndrome, coming on acutely is occasionally encountered Radicular pains myoclonic movements in various parts of the body especially in the abdominal muscles are common symptoms In some patients particularly in children insomnia rather than lethargy occurs and a reversal of the sleep formula is seen Hiccough may be a prominent symptom

The leukocytes in the blood are usually slightly to moderately increased The number of cells in the *spinal fluid* varies In some cases the count is practically normal and in others it goes as high as 400 Thirty to forty cells is a common finding The cells are usually lymphocytes The most important finding in the spinal fluid is the increase in the sugar content The protein is also increased and not infrequently an alteration in the colloidal gold curve in the middle zone is found The urine often shows signs of nephritis which is in a few cases a contributing cause of death Delirium excitement maniacal states and one suggestive of Korsakoff s psychosis may be seen Herpes is an uncommon complication of epidemic encephalitis Slight optic neuritis may be seen There are undoubtedly many mild and abortive types of the disease just as there are of acute anterior poliomyelitis The disease has not been pandemic since 1926 although isolated epidemics have occurred since that time neither the clinical course nor the pathology were similar to the disease as originally described

*Diagnosis* —In view of the signs of meningitis the most common mistake in diagnosis is in assuming that tuberculous or some other form of meningitis is present The greatest help in differentiating these two conditions is in the examination of the spinal fluid

It is often extremely difficult to distinguish between acute multiple sclerosis and acute disseminated encephalomyelitis from epidemic encephalitis in fact some instances *of acute disseminated encephalomyelitis may* be due to the virus of encephalitis The presence of definite pyramidal tract signs will usually point to these conditions rather than to epidemic encephalitis Neurosyphilis especially if producing lethargy and cranial nerve palsies often presents a problem in differential diagnosis Occasionally a patient under treatment for neurosyphilis develops epidemic encephalitis Cerebral neoplasm often presents difficulties in differential diagnosis Uremia and diabetes can usually be distinguished by a complete survey of the case

*Prognosis* —The mortality varies from 5 to 25 per cent The duration of the acute symptoms varies from a few hours to a *number of months The longer the patient* has remained ill at the onset, the more likelihood there is that he will develop evidence of chronic encephalitis This is not however, a constant rule The most foreboding thing that happens in the course of the illness is signs of bulbar paralysis, frequently resulting in sudden death Many patients never make a complete recovery, but immediately develop signs of Parkinsonism or other evidences of chronic encephalitis Depending on the predominance of symptoms types of the diseases are classified as lethargic, hyperkinetic myostatic meningitic psychotic bulbar myelitic and neuritic

The percentage of cases which develop *signs of chronic encephalitis* is high The commonest syndrome of chronic encephalitis is Parkinsonism which may begin during the acute illness or which may not appear for years afterward Various types of irregular movement such as chorea athetosis facial tic or spasms are occasionally symptoms of the chronic stage of the disease The pupils not infrequently are irregular unequal and either dilated or contracted Loss of accommodation and at times an Argyll Robertson pupil may be observed So-called oculogyric crises in which the eyeballs *become fixed in one* position for a few minutes to hours are very disturbing symptoms in the chronic stage Tachypnea

seen in pseudosclerosis and rigidity is usually absent In pseudosclerosis a peculiar greenish discoloration of the corneal margins is frequently observed This has been called the Kayser Fleischer ring or Fleischer-Strumpell ring The speech and type of tremor may suggest multiple sclerosis but nystagmus optic atrophy pyramidal tract signs and alteration of the colloidal gold curve test are absent

## EPIDEMIC ENCEPHALITIS

The condition which we now commonly refer to as epidemic encephalitis was first described by von Economo under the title of *lethargic encephalitis* There is much in medical history to indicate that the disease has been prevalent in the past and has been described under various titles After its appearance in Europe, in 1917, the disease spread over the entire world The first cases in the United States occurred toward the end of 1918 and the early part of 1919 The first great epidemic of encephalitis came after the severe and widespread epidemic of influenza The type of the disease varied in different years It is not contagious in the ordinary sense of the word and while more than one case has occurred in a family even this is uncommon The writers have never seen a case develop in a hospital ward either among other patients or among the doctors and nurses handling cases of epidemic encephalitis

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lead to mistakes in diagnosis such as hysteria or dementia praecox. The deep reflexes are frequently unaltered and Babinski's sign a great rarity. Involvement of the sphincters does not usually occur, but incontinence of urine is occasionally seen probably due to the stupor of the patient. Impairment of accommodation and loss of pupillary reaction are frequently seen in the acute stage. A paralysis agitans syndrome coming on acutely is occasionally encountered. Radicular pains, myoclonic movements in various parts of the body especially in the abdominal muscles, are common symptoms. In some patients particularly in children insomnia rather than lethargy occurs and a reversal of the sleep formula is seen. Hiccough may be a prominent symptom.

The leukocytes in the blood are usually slightly to moderately increased. The number of cells in the *spinal fluid* varies. In some cases the count is practically normal and in others it goes as high as 400. Thirty to forty cells is a common finding. The cells are usually lymphocytes. The most important finding in the spinal fluid is the increase in the sugar content. The protein is also increased and not infrequently an alteration in the colloidal gold curve in the middle zone is found. The urine often shows signs of nephritis which is in a few cases a contributing cause of death. Delirium excitement maniacal states and one suggestive of Korsakoff's psychosis may be seen. Herpes is an uncommon complication of epidemic encephalitis. Slight optic neuritis may be seen. There are undoubtedly many mild and abortive types of the disease just as there are of acute anterior poliomyelitis. The disease has not been pandemic since 1926 although isolated epidemics have occurred since that time neither the clinical course nor the pathology were similar to the disease as originally described.

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It is often extremely difficult to distinguish between acute multiple sclerosis and acute disseminated encephalomyelitis from epidemic encephalitis in fact some instances of acute disseminated encephalomyelitis may be due to the virus of encephalitis. The presence of definite pyramidal tract signs will usually point to these conditions rather than to epidemic encephalitis. Neurosyphilis especially if producing lethargy and cranial nerve palsies often presents a problem in differential diagnosis. Occasionally a patient under treatment for neurosyphilis develops epidemic encephalitis. Cerebral neoplasm often presents difficulties in differential diagnosis. Uremia and diabetes can usually be distinguished by a complete survey of the case.

*Prognosis*—The mortality varies from 5 to 25 per cent. The duration of the acute symptoms varies from a few hours to a number of months. The longer the patient has remained ill at the onset the more likelihood there is that he will develop evidence of chronic encephalitis. This is not however a constant rule. The most foreboding thing that happens in the course of the illness is signs of bulbar paralysis, frequently resulting in sudden death. Many patients never make a complete recovery but immediately develop signs of Parkinsonism or other evidences of chronic encephalitis. Depending on the predominance of symptoms types of the diseases are classified as lethargic hyperkinetic myostatic meningitic, psychotic bulbar myelitic and neuritic.

The percentage of cases which develop signs of *chronic encephalitis* is high. The commonest syndrome of chronic encephalitis is Parkinsonism which may begin during the acute illness or which may not appear for years afterward. Various types of irregular movement such as chorea athetosis facial tic or spasms are occasionally symptoms of the chronic stage of the disease. The pupils not infrequently are irregular unequal and either dilated or contracted. Loss of accommodation and at times an Argyll Robertson pupil may be observed. So-called oculogyric crises in which the eyeballs become fixed in one position for a few minutes to hours are very disturbing symptoms in the chronic stage. Tachypnea

with signs of hyperventilation are rare manifestations of chronic encephalitis. Behavior disorders and reversal of the sleep formula are known sequels especially in children. Narcolepsy, in many instances is due to chronic encephalitis. Symptoms very suggestive of a psychoneurosis frequently exist for months or years before the patient develops signs, which make it possible to say that the disease is definitely organic and of an encephalitic nature.

*Treatment.*—There is no specific in the treatment of this disease which is largely symptomatic. As yet none of the presently available antibiotics has proved to be of any established value.

## ENCEPHALITIS DUE TO NEUROTROPIC VIRUSES

The encephalitides due to specific viruses possessing a selective affinity for the central nervous system include St Louis encephalitis, Japanese B encephalitis, Eastern and Western equine encephalomyelitis, Venezuela encephalitis, Australian X disease, Russian forest-spring encephalitis and West Nile encephalitis. Although the viruses producing these diseases show certain antigenic relationships and their clinical and pathologic manifestations are often similar they are immunologically distinct. The epidemiology of these virus forms of encephalitis has not as yet been definitely established but the available evidence suggests a widespread animal host reservoir with arthopods such as mosquitoes and ticks as transmission vectors. Sporadic epidemics of the St Louis and equine encephalomyelitis types have been prevalent in the United States particularly in the Western regions.

## ST LOUIS ENCEPHALITIS

From July to October 1933 an epidemic of slightly more than 1000 cases of encephalitis occurred in the St Louis area. The causative agent was found to be a virus pathogenic for mice and monkeys as well as man which was neutralized by the serum of patients convalescing from the disease. The seasonal incidence suggested that the spread of the contagion might be by an insect vector but attempts to reproduce the disease in monkeys and man by mosquitoes presumably infected, were unsuccessful. As yet the exact mode of transmission is not known. Individual susceptibility rather than exposure to infection appears to be the principal factor in determining morbidity.

In the St Louis epidemic, the highest incidence and mortality occurred in the older age groups. The incubation period varied from four to twenty one days. Clinically, the disease was characterized by an abrupt onset of high fever, headache, meningeal signs, mental confusion, drowsiness and other neurologic manifestations such as tremors, speech defects and reflex alterations. Ocular manifestations were very rare. In some cases there was a prodromal period of malaise, chills, "grippe" like pains in the back and neck, nausea, vomiting and abdominal discomfort. Following a stormy course in most cases the temperature fell by lysis within seven to ten days and led to complete recovery in two to three weeks. The majority of deaths occurred within the first week. The mortality was about 20 per cent. Residual sequels so common following the epidemic type of encephalitis were very rare.

The blood count usually revealed a moderate polymorphonuclear leukocytosis (12 000 to 20 000). The spinal fluid was clear but often under slightly increased pressure with an increase in cells (average 50 to 250, lymphocytes predominating). The spinal fluid sugar was normal or slightly increased and the globulin moderately increased.

The essential pathologic findings were severe vascular congestion with occasional petechial hemorrhages, cellular infiltration with monocytes and varying degrees of degenerative neuronal changes. The inflammatory foci were widespread, frequently occurred in the cortex and were not limited to the mid brain or basal ganglia.

Symptoms similar to those of the St Louis epidemic were found in the 1941 epidemic prevalent in the Dakotas, Minnesota, Montana and Nebraska.

## JAPANESE B ENCEPHALITIS

This disease occurs only in Japan and clinically is similar to the St Louis type but differs serologically. The virus is probably transmitted by mosquitoes although the host animal reservoirs are not known.

## EQUINE ENCEPHALOMYELITIS

In 1932, 3 cases of encephalitis occurring in men who had worked in close contact with sick horses during an epizootic of equine encephalitis were reported from California. Although the disease occurred in epizootic form in widespread areas of the United States during the subsequent years no further human cases were recognized until the summer of 1938 when minor epidemics closely coinciding with the appearance of epizootic in the respective region occurred in Southern California, Minnesota, Wisconsin, Southeastern Massachusetts and Rhode Island. The etiologic agent proved to be a virus of which two immunologically distinct types, the Eastern and Western, were recognized. The virus reservoirs are possibly birds and insects. It has been demonstrated that the virus can be transmitted by mosquitoes (Aedes aegypti).

The common clinical features are an abrupt onset of headache, malaise and nausea with fever (100° to 104°) and drowsiness. Meningeal

signs convulsions, stupor respiratory failure and death develop rapidly Some cases show a transient remission with a more severe recrudescence of symptoms seven to ten days later The average duration of illness was seven days The Eastern form is much more severe than the Western, the mortality in the former being 75 per cent against 5 per cent in the latter In the Massachusetts epidemic 70 per cent of cases occurred in children Sequels in the form of mental retardation hemiparesis aphasia and emotional instability are frequent following the Eastern form but rare following the Western

The blood count usually shows a polymorphonuclear leukocytosis (10 000 to 60 000) The spinal fluid pressure is normal or slightly increased with a cell count of 500 to 1000 usually polymorphs The spinal fluid protein is increased

Pathologically the disease is characterized by perivascular cell infiltration with extreme degenerative changes in the neurones

## VENEZUELAN ENCEPHALITIS

A disease clinically similar but immunologically distinct from equine encephalomyelitis is reported to have occurred in Venezuela in 1938

## AUSTRALIAN X DISEASE

This type of encephalitis occurred as an epidemic in children in New South Wales in 1917 1918, 1922 and 1926

## RUSSIAN FOREST-SPRING ENCEPHALITIS

This form of encephalitis occurs in Russian forest workers during the late spring and early summer months It is due to a specific virus distinct from the St Louis type but antigenically related to the Japanese B virus Virus reservoirs have been found in rodents and the disease is quite likely transmitted by ticks

## WEST NILE ENCEPHALITIS

This disease has been reported from Africa It is due to a specific virus closely related immunologically to the other types

## TREATMENT OF THE VIRUS ENCEPHALIDES

At present there is no specific treatment and symptomatic therapy is indicated Headache and the meningeal signs may be alleviated by lumbar puncture and by hypertonic solutions The sulfa preparations and the presently available antibiotics are of no value Convalescent serum has not proved to be of value While vaccines have been produced for some types their worth has not been established

## SECONDARY ENCEPHALITIS

Encephalitis may occur in the course of almost any acute infectious disease but particularly following the exanthemata such as measles chickenpox mumps scarlatina and pertussis It may follow rabies or smallpox vaccination Clinically such encephalides are characterized by fever clouding of consciousness and other mental symptoms drowsiness, convulsions paralysis and other neurologic signs Treatment is symptomatic and there are frequently sequels such as mental retardation behavior disorders convulsions and residual neurologic defects

Toxic substances such as lead carbon monoxide and arsenic may produce an encephalophathy with symptoms and sequels similar to those found in the secondary encephalitis

## EPILEPSY

Epilepsy is a loss of consciousness which may be momentary called *petit mal*, or which may be prolonged for minutes or more and be accompanied by a convulsion (*grand mal*) Furthermore certain mental states such as amnesia automatism or periods of excitement may take the place of the fit (Psychomotor seizure) There are two main groups of epilepsy The symptomatic in which epilepsy is a symptom of some underlying neurologic disorder such as brain tumor or paresis and idiopathic or essential epilepsy in which no cause for the seizures can be detected In the so called idiopathic type of the disease very little indeed has been found in the brain to account for the attacks Involvement of the ammon s horn occurs frequently but is probably a result of the disease and not the cause of it Occasionally one finds thickening of the pia and an excessive collection of fluid over the cortex The ventricles may be dilated and drawn to one side Occasionally evidence of an attack of encephalitis may be found but this is not common The cerebrospinal fluid shows no constant alteration and the pressure is normal or low

*Etiology* —Most cases of idiopathic epilepsy develop before the age of twenty five years and a large percentage appear before the age of six years or before puberty Convulsions occurring after twenty five or thirty years of age should always cause a vigorous search to be made for evidence of gross intracranial disease Evidence of old injury to the brain various toxemias, and

alcohol should be considered as the possible cause Epilepsy may occur late in life on an arteriosclerotic basis and is referred to as *epilepsia tarda* The most important etiologic factor is heredity which in some series, may be as high as 50 per cent Heredity may not be direct, but may be passed on as an evidence of *instability* *The incidence* of epilepsy due to congenital syphilis is probably not more than 1 per cent Convulsions of course may occur in individuals who have congenital syphilis either of the paretic or meningo encephalitic type Alcoholism in the parents particularly if the child is conceived during a debauch is supposed to account for a number of epileptics Difficult or prolonged labor especially with instrumentation is probably an important etiologic factor in the production of convulsions At least 10, and perhaps as high as 20 per cent of normal babies have blood in the spinal fluid after birth and this may later serve as a predisposing factor in the production of convulsions In certain cases of prolonged labor with asphyxiation changes may occur in the cortical cells which may later on be a cause of epilepsy The influence of a severe fright in the production of convulsions is probably not great but we have seen a few cases in which the history at least indicated that the first fit occurred after a severe fright Emotional turmoil may be a precipitating factor Convulsions frequently occur in susceptible children in the early stage of infectious diseases especially scarlet fever and an infectious disease may produce changes in the brain which later on predispose the individual to convulsions An occasional case of epidemic encephalitis develops epilepsy as a sequel Convulsions may ensue as the result of allergic reaction to food and other articles but in our experience allergy is rare as a cause

The importance of the so-called reflex epilepsy has been greatly overestimated A few patients suffering from intestinal parasites undoubtedly have convulsions which are probably *not reflex*, but due to the toxemia produced by the infestation and while the removal of the worms may cause a cessation of the fits, they may not be entirely arrested

Various intoxicants may produce convulsions, the commonest one being alcohol There are quite a few people who have fits when they indulge excessively in alcohol and as long as they refrain from use of this drug they do not have convulsions Repeated attacks of delirium tremens may produce changes in the meninges and cortex of sufficient degree to cause recurring spasms In France, where absinthe drinking was common, the so-called absinthe epilepsy was seen Epileptics are not usually alcoholic, but if an epileptic does take alcohol either moderately or to excess he will have a greater number of convulsions than if he refrained from the use of the drug

The occurrence of seizures during pregnancy while often attributed to a toxemia as the result of that state, is quite often due to epilepsy Epileptiform seizures may occur after severe head injury The percentage of cases however which develop a convulsive state is not great probably about 7 per cent It has been proved experimentally that in animals which have been subjected to head trauma convulsants such as absinthe or camphor will more readily cause fits This is an important point from a medico legal standpoint as well as from other considerations Scarring of the brain, with distortion of the ventricular system especially with the pulling of the ventricle toward the side of the lesion occurs In the histories of *epileptics it is* common to see scarlet fever diphtheria or other infections given as the cause of the first convulsion Gross organic disease of the brain such as tumor syphilis abscess and vascular disease sometimes cause fits especially if the person is predisposed by heredity Generalized convulsions however are not common in gross organic disease of the brain except paresis

Chronic poisonings (as lead) heart block (Stokes Adams syndrome) uremia and tetany may all produce convulsions as will also hyperinsulinism The occurrence of spasms during infancy from any cause whatsoever is frequently the forerunner of epilepsy later in life

While it is readily seen therefore that there are numerous factors which must be considered in arriving at a diagnosis in a

patient who has convulsions it is quite true that there are many patients in whom no cause for the fits can be found

While Jacksonian fits are frequently due to organic disease of the brain such as a tumor or syphilis they also occur in idiopathic epilepsy Jacksonian fits do not in themselves indicate an operable lesion The history shows that the fit often begins on one side and may even be localized there for sometime before spreading to the other

*Symptoms* — The vast majority of epileptic seizures come under the heading of *petit mal or grand mal* The attack of petit mal or minor epilepsy is characterized by a sudden loss of consciousness which occurs without warning without a convulsion and without the patient falling to the ground the whole affair lasting but a few seconds The minor attacks may come on at any time and often *escape notice of the family As a rule the* patient suddenly stops what he is doing stares straight ahead the face becomes pale and there may be a slight movement of the tongue and lips or eyes and more rarely of an extremity the patient may yawn make chewing or swallowing movements and then frequently rubs his face and the fit is over The patient often refers to these attacks as bilious or dizzy spells The epileptic may have an enormous number of attacks of petit mal in one month Petit mal attacks may occur without major fits but as a rule are associated with them The patient suffering from major attacks may have them disappear under treatment only to be replaced by minor spells

*Pyknolepsy* is a type of minor epilepsy characterized by the great number of attacks It usually occurs in children and in many cases the attacks often abruptly disappear never to return but in some cases grand mal attacks eventually ensue The ordinary anti-epileptic remedies have little if any effect on attacks of pyknolepsy

Whether or not *narcolepsy* is a variety of epilepsy is a disputed point It is a condition in which an irresistible tendency to sleep occurs the sleep apparently being natural It is likely to occur during any monotous activity but it may occur while the patient is walking along the street riding in a conveyance or playing games The narcoleptic frequently under emotion, especially laughter, has extreme weakness of the legs which give way and he sinks to the ground powerless, but usually conscious (cataplexy) Narcolepsy may follow epidemic encephalitis Ephedrine Benzedrine or Dexedrine by mouth in moderate doses daily has given some favorable results in the treatment of narcolepsy

The grand or major attack in epilepsy is the most dramatic part of the disease and is often preceded by a change in disposition of the patient or by vertigo As a rule however it begins suddenly with unconsciousness In about one-half the cases it is preceded by a warning or *aura* which is a subjective sensation referable to various parts of the body or special senses One of the commonest of aurae is that referable to the epigastrium The patient says he has a *peculiar feeling in the pit of the stomach* which ascends to the head and when it reaches the eyes he becomes unconscious He may have a visual aura which may resemble the scintillating scotomata of migraine He may see animals bright lights or something which appears in the distance which rushes toward him producing unconsciousness when it strikes him Sometimes the aura is referable to an extremity or one side of the body and consists of a paresthesia or dysesthesia The aura may consist of tinnitus which seems to begin in the distance and rapidly approaches the person The next step in the fit is a *cry* or guttural noise which occurs in about half of the cases The cry is often loud and piercing and rather terrifying to the listener If standing the epileptic *falls* and frequently injures himself Many epileptics pitch suddenly forward or backward and as a result this type of case has many injuries and scars on the face In the tonic phase of the *fit* the entire body becomes rigid in extension If the tongue or cheek is caught between the jaws as they are closed it may be severely bitten The patient may assume an attitude of opisthotonos and occasionally one of decerebrate rigidity The pupils will contract then dilate and become fixed to light the muscles of respiration being fixed in the tonic phase respiration is impossible and the patient becomes cyanotic The *tonic*

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of a religious nature. For the maniacal phase after a fit the patient is usually amnesic. This condition may last from a few hours to weeks. Occasionally an automatic state may be a substitute for a fit. About 10 per cent of epileptics after a fit are quarrelsome, destructive, may commit criminal acts, and often wander away.

Epilepsy is occasionally used as a defense for crime but all epileptics who commit crimes are not irresponsible. It might truthfully be said, however, from a medical standpoint that in most instances an epileptic has reduced responsibility.

*Status epilepticus* is one of the most severe manifestations of epilepsy and a frequent cause of death. In status, which consists of a series of convulsions without consciousness being regained between attacks, the patient may have from two to hundreds of seizures. There are some epileptics who apparently have their fits only in series and who may then go some time without having any major attacks. After status, stupor becomes deep, the temperature rises to 103° to 106° F. or higher, the breathing becomes noisy and occasionally Cheyne-Stokes, the heart action may become irregular, and edema of the lungs ensues and frequently causes death. Trophic sores are common in some epileptics who have status. Occasionally status epilepticus is limited to one side of the body, when the term *status hemiepilepticus* is applied. Occasionally after a convulsion or particularly after a series of convulsions an exhaustion paralysis of one side may occur; this paralysis usually clears up in a few hours to days.

In *epilepsia partialis continua* the attacks are limited, as a rule, to an extremity or a part of an extremity, or to the face and tongue. This condition is usually due to gross organic disease of the brain, such as syphilis, tumor or encephalitis, but may occur in idiopathic epilepsy. The attacks of epilepsy may be diurnal, nocturnal or both.

The frequency of the fits varies greatly from one every few months to numerous fits daily. The fortunate epileptic is he who has only an occasional major attack and that at night. The individual who has petit mal spells is likely to have numerous ones. As he grows older, the frequency of his fits, however, may be reduced.

Atypical fits or epileptic variants occur. Among them abdominal epilepsy, characterized by paroxysms of acute abdominal pain and electroencephalographic abnormalities, have been described (Moore).

*Diagnosis.*—In arriving at the diagnosis of epilepsy, which can be satisfactorily done in the vast majority of cases by the history, it is sometimes necessary to observe a convulsion, especially if the question of hysteria enters into the picture. Hysterical convulsions, which are most uncommon in this country, are the opposite of the epileptic ones. They occur during the daytime; the typical aura and cry are absent; the patient practically never injures himself; the tongue is not bitten; the sphincters do not relax, and the tonic and clonic phases of the ordinary epilepsy are lacking. The pupils react to light, the conjunctival reflex is preserved and the Babinski sign is never seen. The patient does not sleep after an hysterical fit, does not vomit and, the atmosphere being cleared by an attack, usually feels better. Strong suggestion may stop the attack, which also will cease if the patient is left alone. While the term hystero-epilepsy is not accepted, some epileptics have hysterical fits as well. The later in life the first attack of epilepsy begins, the more thorough should be the search for conditions capable of producing convulsions, especially a cerebral neoplasm, which may exist for years without localizing signs. The confused state with a fear of fainting complained of by many psychoneurotics may also be mistaken for minor epilepsy.

The relation of infantile convulsions to epilepsy is an important one. Although every patient who has infantile convulsions does not become an epileptic, many of them do.

*Electro-encephalography in Epilepsy.*—Electro-encephalography is of value in the diagnosis of some cases of epilepsy, particularly when the clinical description of the seizure may not be clear, when the seizures are infrequent, or when they cannot be clinically differentiated from hysteria. A routine electro-encephalogram is of value in the diagnosis in 58 per cent of patients

*phase* lasts from a few seconds to a minute or two, and is followed by the *clonic stage* which lasts from a few seconds to four or five minutes The head jerks violently, the muscles of the extremities are vigorously contracted and relaxed and are the seat of electric-like movements The contraction of the muscles of mastication causes a frothy saliva to exude from the mouth and, if the tongue lips or cheeks have been bitten the saliva is blood tinged Dislocation of joints especially the shoulder, is not infrequently produced in this phase The facial muscles twitch the eyeballs roll around and respiration is noisy The pupillary reflexes remain lost in this phase and the deep reflexes are obtained with difficulty The pulse is small and rapid and the blood pressure, which may be slightly elevated at first drops during the spasm The Babinski reflex may frequently be obtained after the convulsion Hemorrhages may occur in various parts of the body especially into the brain and conjunctiva An occasional convulsive movement may persist for some minutes after the severity of the fit has subsided The epileptic usually sleeps after an attack the period of sleep may vary from a few minutes to a number of hours Quite often after an attack and either before or after the stupor the patient performs purposeless automatic acts in which he attempts to undress or fumbles with his clothes When the patient recovers consciousness he practically always complains of headache which may last for hours Vomiting is an occasional symptom after a fit As a rule there is complete amnesia for the spell and this period may last a number of days during which the patient may wander away and perform automatic deeds (fugue) Owing to the severity of the muscular contractures the epileptic usually has muscular soreness after a fit The temperature is slightly elevated and the patient passes considerable urine after a spell and it often contains albumin and casts which are not found on subsequent examinations but which may give rise to confusion in the diagnosis Relaxation of the sphincters especially the urinary sphincter occurs either during the tonic or clonic stage It does not occur in all attacks but is a symptom at some time in the history of most epileptics

In an attack of the so called rare *epilepsia procursiva* the patient suddenly begins to run usually forward and at the end of a few seconds running he may become confused or may fall and have a fit

Many gradations of epileptic fits occur between the attack of petit mal and the grand seizure Some become unconscious and pitch forward and that is the entire attack others fall and have a few convulsive movements and the attack is over Some have what they themselves call the "jerks," in which violent muscle spasms occur, often of sufficient severity to throw the patient to the ground and as a rule without unconsciousness These muscle spasms are accompanied by considerable pain

The disposition of an epileptic is sometimes trying He may be noncooperative quarrelsome and pugnacious given to attacks of depression suspicious hypersensitive and may have a violent temper He is frequently loquacious and will talk unceasingly often in a monotonous tone of his complaints Some are pathologic liars and egotistic Their memory is sometimes poor and they tend to become asocial However there are many epileptics who show no outstanding defects in personality and behavior and if their fits are controlled they are able to make a satisfactory adjustment to society Mental deterioration sometimes ensues and in the end mental dilapidation may be complete Mental disturbances may occur before or after a seizure or the so called *psychic equivalent* may be the manifestation of a fit In the psychomotor attacks the patient may exhibit abnormal and psychotic behavior for which there is usually an amnesia on recovery Fortunately the psychic equivalent is not common but in it the patient may develop a homocidal mania in which he may kill one or a number of people Murders committed in this phase are often extremely brutal The presently available evidence suggests that the psychomotor disturbances arise from a focus in the anterior temporal lobe After any variety of attack the patient may be violent confused or delirious He also frequently suffers from delusions and hallucinations especially the latter and the symptoms frequently are

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important adjuncts in the treatment of epilepsy

In the past, many different varieties of diets have been recommended for the epileptic Today the epileptic is permitted almost any well balanced diet his palate craves A ketogenic diet and dehydration have been advocated by some The ketogenic diet starvation and dehydration are more likely to cause beneficial results in children in whom remissions are common without any method of treatment The good obtained from these methods of treatment in adults is meager

Many drugs have been recommended for the treatment of epilepsy Until recently the drug most in vogue was phenobarbital (luminal) The dose will vary with the age and weight of the patient but for the ordinary young adult 1½ to 6 grains (0 1 to 0 4 gm ) may be prescribed daily If more than 1 grain is given daily it should be in divided doses, with the largest dose at bedtime If given to excess it will produce mental dullness slurred speech pronounced lethargy and occasionally a rash which simulates scarlet fever Myerson and others have advocated giving benzedrine sulphate (amphetamine) to their patients who require large doses of luminal in order to conteract the lethargy and dullness If luminal is used in the treatment of epilepsy it should not be suddenly withdrawn because status epilepticus may ensue If only one dose of luminal is given a day it is more convenient for the patient to take it at bedtime Dilantin (sodium diphenyl hydantoinate) was introduced by Merritt and Putnam in 1938 as a drug which had a high anticonvulsant action with little or no hypnotic or sedative effect This drug has proved to be of value in many cases in which the seizures were not adequately checked by phenobarbital It appears to be of more value in cases with grand mal and psychomotor equivalents than in petit mal The dose varies from 1½ grains to 6 grains (0 1 gm to 0 4 gm ) a day depending on the frequency and severity of the seizures In patients previously taking phenobarbital the transition to dilantin should be gradual otherwise the frequency of attacks may temporarily be increased Toxic symptoms such as ataxia, dizziness, mild nausea tremor, blurred vision diplopia dermatitis and hyperplasia of the gums may occur We prefer to limit the use of this drug to those cases not satisfactorily controlled by phenobarbital Until the advent of luminal the remedy most prescribed was bromide five to 30 grains (0 3 to 2 gm ) or more may be prescribed three or four times daily Prolonged administration may give rise to toxic symptoms, the chief of which are dermatitis mental lethargy and psychotic manifestations Mensantoin (3 methyl-5 phenyl 5 ethylhydantoin) is helpful in some cases with grand mal seizures cases that cannot be controlled by dilantin It has some undesirable toxic effects the most serious of which is the production of pancytopenia Frequent checks on the blood count are therefore necessary In the treatment of petit mal the drug of greatest value is tridione This drug likewise may give rise to aplastic anemia and agranulocytic angina In some patients it produces an annoying glare phenomenon which while not harmful to vision is still troublesome

The choice of drugs and the dosage must be individualized With a little trial and error experimentation the optimum combination and dosage can be obtained

Operations on the brains of epileptics produce rarely good results A patient who has had epileptic fits for many years beginning on one side of the body or in one extremity and without definite localizing signs between attacks or any other evidence to indicate an intracranial mass lesion should not be operated upon Excision of part of the motor cortex has been tried unsuccessfully In the posttraumatic type of epilepsy with scarring of the brain the excision of the scar has been advised and improvement reported

The treatment of an attack of status is a difficult one Epsom salts should be administered if necessary by a nasal tube and 3 ounces given in 6 ounces of water by rectum The use of sodium luminal intravenously in doses of 5 to 10 grains (0 3 to 0 6 gm ) should be employed and if the attacks still persist a lumbar puncture may be performed Chloral and bromides by

with seizures, while in 42 per cent it is of little or no value

The electrical pattern obtained during an actual seizure is distinctive for each of the three main clinical types of seizures

In the interval between clinical attacks, the electro-encephalogram may record abnormal wave patterns which tend to correspond with the type of clinical seizure manifest in the particular case

*Prognosis* —The prognosis in epilepsy is poor as regards cure but the outlook for life is good

The percentage cured of attacks is small and probably falls between 5 and 10 If the first seizure occurs late in life the outlook is better than if it had happened early A patient with one or two fits a year will naturally respond more favorably than one who has daily attacks Bad heredity also affects the prognosis as does also the history of status epilepticus

*Treatment* —While the treatment of epilepsy offers poor results as far as cure is concerned sufficient and prompt treatment does reduce the number and severity of the fits in a large percentage While it is true that even the most painstaking search for an etiologic factor may produce nothing of importance many conditions may be found which can be remedied and the patient given improved general health as a result

The *prophylaxis* of epilepsy should begin before conception The question of marriage should be individualized Prevention of injuries at birth and their proper treatment if present are important The nervous high-strung child especially he who has had infantile convulsions or such diseases which may be closely allied to epilepsy such as night terrors, sleep walking nocturnal enuresis or the child who has had severe head injury with unconsciousness should be closely observed by the medical attendant and kept in good general health The history of infantile convulsions should call for close observation of the development of the child, who should be treated as a potential epileptic If a child has a convulsion which has no relation to an acute infectious disease, head trauma or other obvious cause treatment should be instituted immediately to cut down the tendency to develop recurring attacks of unconsciousness with convulsions It must be borne in mind that there are many epileptics who having had a few convulsions before the age of six years may have no further attacks until puberty or later

Nothing can be done to cut short an attack once it has begun, although certain patients feel that sometimes they may abort an attack by various maneuvers such as tightly squeezing the extremity in which the aura appears In the attack itself the chief concern should be to prevent injury Some object should be inserted between the teeth to prevent biting of the tongue lips and cheek, such as a spoon or tongue depressor padded with cotton and a bandage A pillow should be placed under the head or the head supported to prevent its being knocked against the floor Sometimes an extremity must be supported because in the severe clonic stage it may be injured by hitting the floor or surrounding objects After the convulsion is over the patient should be watched and prevented from doing automatic acts which are dangerous to himself or others and to see that he does not wander away The epileptic should be allowed to sleep out the fit and no effort should be made to hasten his recovery from the postepileptic stupor

The subject of the epileptics employment is an important one Although in the past it was practically impossible for a known epileptic to keep a job today many are gainfully employed The epileptic should never be allowed to continue work which is obviously hazardous such as working around machinery driving an automobile any job which takes him off the ground railway work in fact anything which might prove to be injurious to himself and others if he had an attack Swimming should not be permitted Work is an excellent thing but excessive fatigue should be avoided Life in the country either on a farm or in a colony for the treatment of epileptics is the best environment for some of these unfortunate people Stimulants which in themselves can cause convulsions should be prohibited Alcohol and tobacco would fall in this group Rigid care of the gastro-intestinal tract and exercise are extremely

be regarded as an aura While the hemianopsia practically always clears up occasionally it becomes permanent Temporary paralysis of an ocular nerve especially the third sometimes occurs and after lasting a few weeks or rarely longer passes away Hemiplegia or hemiparesis paresthesia or dysesthesia limited to one side of the body and aphasia may complicate an attack of migraine Psychotic episodes resembling very much those seen after an epileptic fit such as confusion, maniacal outbreaks and an hallucinatory state are rare happenings but give an added similarity to certain manifestations of epilepsy and migraine *The frequency of the attacks vary from one* or two a month to about the same number a year They may disappear at the menopause

The *diagnosis* of migraine is usually simple especially when the visual phenomena accompany it A case of migraine complicated with a paralytic phenomenon may be mistaken for a tumor or a vascular accident After a patient has had migraine for many years is advanced in years and arteriosclerotic it may be difficult to differentiate between a paralytic state due to hemicrania and vascular disease Sinus disease, syphilis trigeminal neuralgia especially the atypical forms and headache due to eye strain have occasionally to be differentiated Headaches *of psychogenic origin may be confused with* migraine The course of migraine is not easily altered While the patient is free *from pain between headaches they are likely* to recur until the time of the menopause and in many patients persist throughout life Histamine headaches are also usually unilateral and are accompanied by symptoms of vasodilatation on the same side such as edema of the eyelids lacrimation and running of the nose The onset usually is after the age of 50 and the headaches usually come on during sleep

*Treatment* —In the management of a case *of migraine as in epilepsy the initial* step should be to place the patient in the best possible condition of general health and diseased states in any part of the body should be corrected The avoidance of both mental and physical fatigue a definite number of hours sleep nightly and regu*larity in the habits of life are essential* Lennox states that ergotamine tartrate will bring relief in nine tenths of patients and believes *the action is specific for headaches* of migraine type The dose is a 1 cc ampule containing 0 5 mg given intramuscularly and 2 tablets *each containing 1 mg* by mouth hourly until the headache is relieved or 6 tablets taken

*Dihydroergotamine* (DHE 45) *is less toxic* and probably as effective Caffergone can be administered orally but it is questionable *if it is as effective The use of luminal* may be advised between headaches, and it frequently reduces the number and severity of *the attacks If any evidence of allergy can* be found a lead for treatment may be obtained in that way Massive doses of thiamin chloride have been advocated as being beneficial but in our experience the results have been very poor Endocrine therapy has been tried usually with no benefit Abnormal conditions in the gastrointestinal tract should be corrected and the diet should consist of simple easily digestible foods If there is evidence of histamine sensitivity desensitization may be tried

*Headache* may be due to many causes such as sinusitis ocular disease anemia hypertension emotional disturbances various toxemias, brain tumors and other conditions of the nervous system These *conditions are discussed elsewhere*

# THE PERIPHERAL NERVOUS SYSTEM

## NEURITIS

*Definition* —Neuritis may be defined as an infection of a peripheral or cranial nerve However when the etiologic agent is non infectious the term neuropathy is more proper

*Etiology* —The causes of neuritis are trauma pressure as from crutches tight bandages or casts and pressure from tumors intoxication by alcohol lead and arsenic and infectious diseases Chronic focal infection often is an added etiologic factor in cases of multiple neuritis due for *example to alcohol Beriberi* is due to a

rectum have been recommended in the treatment of status but the depressing effect of chloral is great and it should be watched for. It is interesting to observe that in many cases of severe status an extreme degree of dehydration ensues yet the convulsions continue. The patient in status must be carefully watched *for signs of pulmonary edema* and heart failure, and if either one of these complications occurs appropriate treatment should be instituted. It is occasionally necessary to give a general anesthetic to stop status epilepticus. During an attack of status trophic sores on the heels and buttocks not infrequently occur and to prevent this the patient's bed should be changed frequently and padded and the back bathed with alcohol and powdered often. There are many epileptics who have a confusional or delusional episode not only after an attack of status but even after a single fit and it is necessary to confine such a patient *rather closely* to a room in which the windows are protected, dangerous objects removed and the door locked.

The psychotherapeutic treatment of an epileptic has an important place. He *should be encouraged and a continued effort* made to get him to cooperate in his treatment. In some cases the best results are obtained by placing the patient in an institution where he develops a routine and a method of living that is best suited to his disease.

## MIGRAINE

*Synonyms.*—Sick headache. Hemicrania.

Migraine is a periodic headache limited to one side of the head, and accompanied by certain eye symptoms and vomiting. The attack often terminates in sleep.

The most important factor in the *etiology* of migraine is heredity. There is a relationship between migraine and epilepsy; some believe that a person suffering from migraine is more likely to produce epileptic children than an epileptic. This is questionable. Attacks of migraine may cease and be replaced by epilepsy, *or* attacks of the two diseases may alternate. Evidence exists that migraine may be an allergic manifestation. Certain foods have been known to precipitate an attack of migraine in which eosinophilia may also occur. Histamine sensitivity has been *thought to be the cause* of periodic headache of both the migraine and non-migraine type. Indiscretions in diet, worry and exhaustion may serve to initiate an attack. Various endocrine abnormalities have been cited as the *etiologic factor in migraine* but the case has not been proved. Other facts, such as the relation of migraine to menstruation, with its occasional disappearance during pregnancy or lactation or at the menopause have been used to support the theory that the ductless glands are at fault. A theory as to the causation of the attacks is that vascular spasms occur probably secondary to sympathetic instability. Attacks of hemiplegia, of aphasia and of hemianopsia during the attack of migraine lend strength to this theory. Some consider migraine a sensory form of epilepsy. The condition is about twice as common in females as in males.

*Symptoms.*—The attack of migraine is usually ushered in by a general ill feeling, drowsiness, slight pain in the head and dizziness. The appetite may be voracious for a day or so prior to the onset of the attack. *These symptoms may last for a* number of hours and are followed by a severe headache which is limited to one side of the head in the attack although it may be frontal or occipital in location. Some patients have the pain on the same side in *all attacks and in others the locality may* vary. It is an unbearable excruciating type of headache and frequently gives the patient thoughts of suicide. Sometimes the head is tender to touch. The headache lasts from a few hours to two or three days and is practically always accompanied by vomiting. After the acute headache subsides a dull ache may be present for a few hours. There is a distinct periodicity to the attacks *which have a tendency to occur at the* menstrual periods in women. The headache is aggravated by noise, light and confusion and the patient suffering from a migrainous headache prefers to be alone. Visual disturbances are frequent. Hemianopsia may occur and be accompanied by dazzling lights, bright dots or zig-zagging phenomena in the blind fields. In some patients the hemianopsia precedes the headache and can

be regarded as an aura. While the hemianopsia practically always clears up, occasionally it becomes permanent. Temporary paralysis of an ocular nerve, especially the third, sometimes occurs and after lasting a few weeks or rarely longer passes away. Hemiplegia or hemiparesis, paresthesia or dysesthesia limited to one side of the body and aphasia may complicate an attack of migraine. Psychotic episodes resembling very much those seen after an epileptic fit, such as confusion, maniacal outbreaks and an hallucinatory state are rare happenings but give an added similarity to certain manifestations of epilepsy and migraine. The frequency of the attacks vary from one or two a month to about the same number a year. They may disappear at the menopause.

The *diagnosis* of migraine is usually simple *especially when the visual phenomena accompany it*. A case of migraine complicated with a paralytic phenomenon may be mistaken for a tumor or a vascular accident. After a patient has had migraine for many years, is advanced in years and arteriosclerotic, it may be difficult to differentiate between a paralytic state due to hemicrania and vascular disease. Sinus disease, syphilis, trigeminal neuralgia, especially the atypical forms, and headache due to eye strain have occasionally to be differentiated. Headaches of psychogenic origin may be confused with migraine. The course of migraine is not easily altered. While the patient is free from pain between headaches they *are likely* to recur until the time of the menopause and in many patients persist throughout life. Histamine headaches are also usually unilateral and are accompanied by symptoms of vasodilatation on the same side, such as edema of the eyelids, lacrimation and running of the nose. The onset usually is after the age of 50 and the headaches usually come on during sleep.

*Treatment.*—In the management of a case of migraine, as in epilepsy, the initial step should be to place the patient in the best possible condition of general health and diseased states in any part of the body *should be corrected*. The avoidance of both mental and physical fatigue, a definite number of hours sleep nightly and regularity in the habits of life are essential. Lennox states that ergotamine tartrate will bring relief in nine-tenths of patients, and believes the action is specific for headaches of migraine type. The dose is a 1 cc ampule containing 0.5 mg given intramuscularly and 2 tablets each containing 1 mg by mouth hourly until the headache is relieved or 8 tablets taken.

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*Headache* may be due to many causes such as sinusitis, ocular disease, anemia, hypertension, emotional disturbances, various toxemias, brain tumors and other conditions of the nervous system. These conditions are discussed elsewhere.

# THE PERIPHERAL NERVOUS SYSTEM

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*Definition.*—Neuritis may be defined as an infection of a peripheral or cranial nerve. However, when the etiologic agent is non-infectious, the term neuropathy is more proper.

*Etiology.*—The causes of neuritis are trauma, pressure as from crutches, tight bandages or casts and pressure from tumors, intoxication by alcohol, lead and arsenic and infectious diseases. Chronic focal infection often is an added etiologic factor in cases of multiple neuritis due for example to alcohol. Beriberi is due to a

deficiency of vitamin $B_1$ in the diet In alcoholic multiple neuritis, in addition to the intoxication by alcohol and focal infection, deficiency of vitamin $B_1$ plays a major role

*Pathology*.—If a peripheral nerve is diseased or injured, the nerve beyond the point of involvement undergoes pathologic changes, sometimes the nerve proximal to the site of injury degenerates, even as high as the anterior horns The myelin sheath breaks up into lecithin bodies and fat droplets The cells of the sheath of Schwann proliferate and the axis cylinder splits and becomes fragmented These processes ultimately result in scarring and the formation of connective tissue

*Symptoms*.—These vary depending upon the nerve involved Most nerves are mixed, containing both motor and sensory fibers, so that in practically every case of neuritis there is a disturbance of both motion and sensation The greatest discomfort which the patient has is due to the involvement of the sensory part of the nerve producing pain and paresthesias which may be characterized by the patient as burning pins and needles, tingling or a sensation of bugs crawling over the skin Sometimes especially if the median or sciatic nerve is involved intense burning pain ensues and to this condition the term causalgia has been given Movement intensifies the pain and tenderness occurs if the nerve is pressed upon

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*Diagnosis*.—The diagnosis of neuritis should be made only after a careful diagnostic survey of the individual Joint disease simulates neuritis by producing pain limitation of motion and wasting of the muscles, and should be considered, especially if the pain is confined to one extremity or part of one extremity Arthritis of the shoulder or hip and bursitis in these regions are frequently labelled neuritis in the early course of the illness The reflex activity is increased in arthritis and sensory loss and reactions of degeneration do not occur Any affection which involves the posterior roots of the spinal cord is frequently called neuritis or neuralgia Such conditions as spinal syphilis, spinal tumors and disease of the vertebræ are misdiagnosed early and late Tumors along the course of the nerve especially pelvic sarcomas are frequently called sciatica Pressure of a cervical rib on the brachial plexus is sometimes considered as a neuritis arising in the nerve itself

## Multiple Neuritis (Polyneuritis)

One of the commonest forms of neuritis is multiple neuritis which is due in the vast majority of instances probably 90 per cent to chronic alcoholism The amount of alcohol necessary to produce neuritis varies with the individual just as the amount of alcohol needed to bring about intoxication depends upon the person Some individuals especially women whose nervous systems are especially susceptible to alcohol may develop signs of multiple neuritis after what might be considered moderate drinking Most individuals who consume fairly large

quantities of alcohol, eat small amounts of food or practically none at all. This leads to a vitamin deficiency, especially $B_1$, and the lack has a distinct effect on not only the peripheral, but also on the central nervous system.

Other frequent causes of multiple neuritis are intoxication due to heavy metals (especially lead and arsenic), diabetes, diphtheria and virus infections.

The earliest *symptom*, as a rule, occurs in the feet and is a paresthesia which may be of any description. One of the commonest and most characteristic symptoms is a burning sensation in the toes and feet so intense that the patient often places his feet in cold water, even on a cake of ice, to control the painful sensation. Another common habit of the patient suffering from alcoholic multiple neuritis is to keep his feet uncovered at night because the warmth produced by blankets increases the burning feeling. The paresthesias gradually ascend the feet and legs and about this time involve the fingers and hands. Tenderness on pressure over the nerves, the pressure of shoes and of the feet on the ground when the patient attempts to walk are unbearable. The tenderness of the feet is best elicited by squeezing the feet; this produces pressure on the nerves as they are passing between the metatarsal bones. Weakness and ultimately paralysis of the muscles come on, usually more marked in the extensors, but finally involving all the muscles. The toe and foot drop and the finger and wrist drop are the earliest paralyses seen, but if the patient continues to use alcohol, if he has a focal infection or if an acute infection should attack him he may lose power in all four extremities.

The deep reflexes in the arcs of the affected nerves become diminished and then lost. The paralysis, which is a flaccid one, is accompanied by atrophy, changes in electrical reactions and trophic disorders. All forms of sensation become impaired in a case of any severity. The loss of sensation occurs first in the distal portions of the extremities and even in severe cases may not be found above the ankles and the wrists. If the patient can still walk when first seen and has paralysis, he will usually show a *steppage gait*, which is due to double foot- and toe-drop. Occasionally in the so-called pseudotabes type of multiple neuritis the gait may be ataxic. Sphincter disturbances do not occur as a rule. Cranial nerve symptoms, with the exception of involvement of the optic nerves, are uncommon in alcoholic multiple neuritis but occur more frequently in polyneuritis due to infections. In alcoholic multiple neuritis any of the forms of mental disease due to alcoholism may be seen. But there is one, namely *Korsakoff's psychosis*, characterized by confusion, disorientation, marked loss of memory and confabulation, which is most commonly noticed. Korsakoff's psychosis may occasionally be due to other toxemias, to infections and also we have seen the syndrome after head injury. It may take some months for the individual to reach the height of the illness. If properly handled most patients will recover but some will do so incompletely.

The most important phase in the *treatment* of a case of alcoholic multiple neuritis is to discontinue the use of the drug. A high caloric diet rich in vitamins, plenty of fresh air and sunshine are extremely important in the management of these cases. Preparations of vitamin B should be given in large doses both by mouth and parenterally. The patient should be immediately placed in the best health possible and all foci of infection removed. A sponge mattress should be used and a cradle should be placed over the lower extremities to keep the weight of the bedclothes off those parts. If actual paralysis exists, splints should be applied and the extremities affected placed in a neutral position. This is extremely important because if foot- and wrist-drop are permitted to exist for some time, changes take place in the muscles and tendons which may result in contracture so that the patient will find after he has recovered from multiple neuritis that he cannot walk because of contractures at the ankles or knees. Drugs are often necessary for the relief of pain and paresthesias, but care should be taken that the patient should not be given an opportunity to develop a new habit. Opium and its derivatives should be used only after everything else has been tried and failed. A combination of bromides and

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### Sciatica

Sciatica is more frequently seen in males. It frequently is observed after infectious diseases or may be due to chronic focal infection especially in the prostate. It may follow exposure to cold. It may occur after intragluteal medication. It may come on after a heavy lifting or a marked muscular exertion especially in people not used to such exertion. It may be due to herniation of the intervertebral disks. True sciatica is usually unilateral. If double sciatica exists it is imperative to rule out the conditions such as syphilis and tumor of the spinal cord. It may be an occupational disease due to pressure on the nerve due to prolonged sitting.

*Symptoms.*—The onset is usually gradual but in certain infectious cases and in those due to *stretching of the nerve during* physical exertion the signs may come on abruptly. Pain begins as a rule in the buttock and follows the course of the nerve down the back of the thigh, calf, heel and to the foot. While the pain is usually constant it may be paroxysmal and like most pains is worse at night. Coughing, sneezing, jarring and motion aggravate the pain which is usually sharp but may be dull. The patient tries to prevent pain by keeping *the extremity flexed at the ankle and the hip* and if he is in bed he holds the extremity flexed at the knee and abducted. He is likely to stand on the healthy extremity, the gluteal fold is low on the affected side and a scoliosis is usually seen with the convexity toward the diseased area. Anything which stretches the nerve, such as bending forward to touch the floor with the fingers or testing for Lasegue's sign (which is done in the same manner as Kernig's sign) makes the patient *cry out* with pain. Tender points may exist along the course of the nerve. Paralysis and sensory loss are uncommon but the latter especially may occur in the distribution of the nerve. The knee jerk is not affected; in fact, due to the tenseness of the patient, it may be slightly exaggerated. The Achilles reflex is diminished or lost. Muscular atrophy and changes in electrical reactions do not occur except in very rare cases. Trophic and vasomotor signs may be seen.

Most patients will recover although the condition may be very resistant to treatment and persist for months.

As far as the *differential diagnosis* is concerned, a condition should be called sciatica only as a last resort. Careful investigation of the pelvis, rectum and spine with particular search for evidence of syphilis, spinal cord tumors, protrusion of the intervertebral disks, focal infections, evidence of arthritis, especially of the hip and sacro-iliac joint, elimination of flat feet and of arterial disease should be gone into before the diagnosis of sciatica is made.

The most important element in the *treatment* is rest. A combination of bromide and salicylate will quiet the patient and relieve the pain. In view of the fact that the condition may be prolonged, opium and its derivatives should not be used. Heat, either dry or wet, usually gives the patient considerable relief and diathermy over the nerve is sometimes of considerable value. If the pain is very severe 5 to 10 cc. of a 1 per cent solution of novocaine may be injected epidurally in the sacral canal and followed in a few minutes by the injection of 50 cc. of normal sterile saline. Direct injection into the nerve sheath of normal saline or alcohol and stretching of the nerve have been used but usually with poor results. The less stretching and injection done the happier the patient. In rare cases exposure of the nerve and freeing it of adhesions have benefited the patient.

### Peripheral Facial Paralysis (Bell's Palsy, Prosoplegia)

This is probably the commonest type of peripheral neuritis. It is much more frequently seen in the spring and fall and is usually due to exposure and chilling of the face. A facial palsy may be seen in the course of any infectious disease, in ear infection, in tumors of the parotid, tumors in the cerebellopontile angle, syphilis in the cerebellopontile angle and direct trauma to the nerve. It is occasionally the result of operations on the parotid or on the ear. Tetanus, especially when the wound of entrance is about the face, may produce

salicylates will often serve to quiet the patient and to relieve him of pain. If insomnia is present, as it often will be early in the treatment, such drugs as the barbiturates may be tried. The gastrointestinal tract should be carefully regulated.

The consideration of local treatment is important. Baking and physiotherapeutic measures which produce heat will often increase the pain if employed early in the course of the illness. As the pain and paresthesias diminish, light gentle massage to the affected parts should be employed every day and mild electrical treatments, either galvanic or faradic, should be used three or four times a week. It is highly important that the joints in the distribution of the paralysis be passively moved every day and that the tendons about them be lightly manipulated. If contractures have developed an effort should be made to overcome them by stretching, passive movement and by deep massage. If all of these are of no avail tenotomy may have to be done. Even after paralysis of all four extremities has persisted for six to twelve months a fair to perfect recovery is possible.

### Lead Multiple Neuritis

The multiple neuritis of lead is essentially a motor one and sensory symptoms, if present at all, are extremely mild. The ordinary signs of lead poisoning are usually present for some time before those of neuritis develop. The condition usually begins in the upper extremities and is practically always bilateral. The first sign of paralysis is in the extensors of the hand and forearm and gradually the entire extremity is involved. The supinator longus muscle usually escapes. Atrophy and reactions of degeneration occur but fibrillations do not. If the disease progresses the peroneal group of muscles is affected in the lower extremities.

### Postdiphtheritic Multiple Neuritis

The type of palsy occurring after diphtheria is usually limited to the uvula, palate and ciliary muscles. The symptoms are difficulty in swallowing, regurgitation of fluids through the nose and paralysis of accommodation. Some of the other cranial nerves may rarely be paralyzed. The paralysis may occur in the course of the disease or may be postponed for days, weeks or months. Paralysis of a part of an extremity may occur if the diphtheritic infection has taken place in that region.

If the polyneuritis of diphtheria becomes generalized the symptoms due to involvement of the nerves affected will appear. As a rule, pain is not a common symptom but the other signs such as loss of reflexes and of sensation, foot-drop and steppage gait occur. The gait may be ataxic. The outlook is good. Involvement of the cranial nerves, however, is a dangerous thing and sudden death may occur from heart failure or the patient may choke to death.

The *treatment* of diphtheritic multiple neuritis is the same as mentioned for other forms of multiple neuritis.

### Arsenical Multiple Neuritis

Arsenical multiple neuritis presents no outstanding features except that it is usually very painful. Certain skin manifestations such as pigmentation, exfoliating dermatitis, herpes and keratoses on the palms and soles of the feet may be seen.

The *treatment* does not vary from that of other forms of the disease. (See chapter 13)

### Diabetic Multiple Neuritis

The *symptoms* here may be due to involvement of the peripheral nerves or to changes in the cord.

The lower extremities are especially involved and the affection is frequently of the tabetic type. Alcohol sometimes plays a contributing role in this condition.

Other conditions may produce multiple neuritis such as carbon monoxide poisoning, beriberi, leprosy and so called pink disease or *erythredema polyneuritis*. It has also been called *acrodynia*. The latter condition is usually seen in children and is frequently accompanied by insomnia, restlessness and swelling and redness of the fingers and toes and possibly also trophic conditions, even gangrene.

### Polyneuronitis

*Definition.*—Infectious involvement of the entire neuron is called neuronitis. The *symptoms* resemble those seen in multiple neuritis but cranial nerve involvement, especially of the seventh nerve, is a common additional sign. Bulbar symptoms frequently are seen and may produce sudden death. Often the proximal muscles are more involved than the distal. Sensory disturbances may be slight or absent. Examination of the spinal fluid often shows an increased protein content without any increase in the number of cells (albumino-cytologic dissociation of Guillain and Barré). The condition usually runs a benign course. The treatment is symptomatic.

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*Symptoms*.—The onset is usually gradual but in certain infectious cases and in those due to stretching of the nerve during physical exertion the signs may come on abruptly. *Pain begins as a rule in the* buttock and follows the course of the nerve down the back of the thigh, calf heel and to the foot. While the pain is usually constant it may be paroxysmal and like most pains is worse at night. Coughing sneezing jarring and motion aggravate the pain *which is usually sharp but may be dull*. The patient tries to prevent pain by keeping the extremity flexed at the ankle and the hip and if he is in bed he holds the extremity flexed at the knee and abducted. He is likely to stand on the healthy extremity the *gluteal fold is low on the affected side and a scoliosis is usually seen with the convexity* toward the diseased area. Anything which stretches the nerve such as bending forward to touch the floor with the fingers or testing for Lasègue's sign (which is done in the same manner as Kernig's sign) makes the patient cry out with pain. Tender points may exist along the *course of the nerve*. Paralysis and sensory loss are uncommon but the latter especially may occur in the distribution of the nerve. The knee jerk is not affected in fact due to the tenseness of the patient it may be slightly exaggerated. The Achilles reflex is diminished or lost. Muscular *atrophy and changes in electrical reactions* do not occur except in very rare cases. Trophic and vasomotor signs may be seen.

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facial paralysis. Facial diplegia is usually due to neurosyphilis at the base, to polyneuronitis and to encephalitis. Occasionally facial diplegia is seen in myasthenia gravis and *muscular dystrophy*. *The weakness of* the face which occurs in bulbar palsy is chiefly in the lower half. A lesion in the pons at the level of the seventh nucleus will produce facial paralysis of the peripheral type, but signs indicative of pontine rather than peripheral disease will be present.

*Symptoms.*—The symptoms are paralysis of the muscles on one side, which is flattened. The corner of the mouth droops and the face may seem drawn to the normal side. The wrinkles and folds normally present on the affected side will be smoothed out either in part or entirely; the eye cannot be closed and the palpebral fissure is wider than normal. Voluntary movement on the affected side is impaired and this may vary from slight weakness to total paralysis. *The patient has difficulty* in chewing because food has a tendency to collect between the gums and the cheek. He frequently drools at first and has slight difficulty in speaking. Because the blinking reflex is lost and there is a relaxation of the lower lid, tears often flow from the eye on the affected side. The loss of reflexes is due to involvement of the motor part of the arc. If the chorda tympani is involved there is a disturbance of taste on the side of the lesion on the anterior two thirds of the tongue. Occasionally herpes of the internal auditory meatus and the auricle with pain in these parts may be a part of the picture (syndrome of the geniculate ganglion). In this there is deep-seated pain in the ear and the mastoid region and occasionally lymphocytosis of the cerebrospinal *fluid*. Occasionally the eighth nerve is involved. Sensation is not affected in the ordinary type of Bell's palsy. In ten days to two weeks after the onset of paralysis, changes in the electrical reactions may occur. These changes may vary *from slight reduction* in contractility to faradism to complete reactions of *degeneration*.

*Diagnosis.*—The most important consideration in the diagnosis of Bell's palsy is to differentiate it from a paralysis of the face of central origin which is usually a part of the picture of hemiplegia, in which condition only the lower part of the face is involved. The tongue deviates to the paralyzed side. Electrical reactions are not affected. The *muscles may move well during emotionalism*. Furthermore in hemiplegia the rest of the same side of the body will be affected.

In bilateral facial paralysis, syphilis, polyneuronitis and encephalitis should be considered from a diagnostic standpoint. If syphilis is to blame, involvement of the eighth nerve may also be seen.

*Prognosis.*—The prognosis in facial paralysis naturally depends upon the cause. If it is the ordinary type due to exposure, the chances for a complete recovery are good. The most valuable aid in prognosis is the reaction of the nerve to electricity two weeks after the onset. The milder the changes to faradism or galvanism, the better is the prognosis. Mild cases will do well in three to six weeks, whereas severe cases may last from three months to one year. If the nerve has been cut during an operation or if involved by a parotid tumor, the outlook is not good. Many patients will recover with contractures, especially those who are treated too vigorously by local measures. Associated movements may be seen on the side of the face which has recovered partially from a Bell's palsy; for example, when a patient winks the eye on the affected side the angle of the mouth draws up and *vice versa*. The reason for this is probably misdirection of the regenerating fibers. Years after a Bell palsy has cleared up facial spasm may be noted on the affected side.

*Treatment.*—The eye should be protected with a patch and washed out frequently with warm boric acid. Small to moderate doses *of sodium salicylate and sodium iodide* should be given and continued for two or four weeks. If there is much drooping on the weakened side this may be strapped up with adhesive. Ten days to two weeks after the onset of paralysis electrical treatment should be initiated on alternate days. If faradism produces a response, that type of electricity should be used; if it does not, galvanism should be employed. On the alternate days mild gentle massage will aid in recovery. As soon as voluntary movement begins to return the number of local treat-

ments should be reduced and when further movement has been established all local treatment should be stopped Treatment should be persisted in for at least six months after the onset, and even after six months of paralysis some cases may make a good recovery Anastomosis of the central end of the hypoglossus or of the spinal accessory with the distal stump of the facial has been tried Neither type of anastomosis is as a rule successful

### Hemifacial Spasm

This condition may involve either the entire facial nerve or one of its branches The movements are painless and resemble those produced by electrical stimulation of the nerve It occasionally occurs without any detectable cause but may be symptom of pressure on the nerve as for example by a tumor in the angle It has been known to follow years after an ordinary Bell palsy

*Treatment* should depend on the cause if none is discoverable psychotherapeutic procedures injection of the nerve with alcohol or partial section of it may be tried but the results are usually disappointing

### Progressive Hemifacial Atrophy

This is a condition which usually begins before puberty is more common in females and more frequently involves the left side of the face The atrophy is first noted in the skin usually at the external angle of the orbit or at the angle of the mouth, and then gradually spreads until it involves the entire side of the face The skin becomes thin fat disappears and later on the underlying muscles and bones become atrophic but actual paralysis and reactions of degeneration do not occur The corresponding side of the tongue even of the soft palate may become atrophic Changes in the hair and of the sweat secretion on the side of the face involved may be found There is neither loss of sensation nor disturbance of taste The cause of this condition is unknown When it occurs in syringomyelia the typical dissociation loss of sensation will be found The condition has been attributed to trauma and may have an important medico legal aspect

### Hemifacial Hypertrophy

Facial hemihypertrophy is an extremely rare condition in which the soft tissue and the bones on one side of the face hypertrophy This may occasionally be found associated with enlargement of one entire side of the body

## NEURALGIA

*General Discussion* —Neuralgia is usually a symptom and not a disease It consists in paroxysmal attacks of pain in the course of a sensory nerve If the neuralgic condition is hysterical in origin it would properly be called psychalgia The most common form of neuralgia is trigeminal (tic douloureux or trifacial neuralgia)

### Trigeminal Neuralgia

Trifacial neuralgia (tic douloureux) is most frequently seen in patients in middle or advanced life Its cause is not known The pain is in the distribution of the fifth nerve If confronted with a patient suffering from pain in the face either in one or all of the branches of the fifth nerve, it is important to rule out conditions which may either by pressure or reflexly cause pain in the area of the trigeminal nerve Tumors in the angle tumors of the Gasserian ganglion diseases of the teeth or the sinuses basilar syphilis and general toxemias or infectious especially malaria, should be considered

*Symptoms* —The pain will obviously be in the distribution of the branch involved but it may spread to the entire supply of the trigeminal nerve Occasionally the pain is bilateral The pain occurs suddenly, is excruciating burning and violent It may last a few seconds or minutes and occurs paroxysmally After a number of attacks in the course of days the pain may subside and disappear for weeks or months During an attack the patient holds the face and head in a set manner, because opening the mouth talking chewing or swallowing may bring on an attack of pain Washing the face or exposure to cold may also bring on an attack Flushing of the skin, and an abnormal flow of tears or saliva and local sweating may be seen Tic like movements of the face smacking of the lips and movements of the jaw may occur The tender points or *trigger zones* so called because irritation of them may bring on an attack, are found along the course of the nerve The symptoms are usually more marked in the daytime

*Diagnosis* —The diagnosis is made chiefly from the conditions mentioned in the fore-

going remarks The presence of sensory findings will rule out organic affections of the ganglion and of the roots of the nerve The pain of *Sluder s neuralgia* is not limited to the fifth nerve, and has a tendency to radiate to the shoulder the importance and frequency of this has been greatly over estimated In *glossopharyngeal neuralgia* the pain radiates from the pharynx to the side of the neck and to the ear The tonsil may act as a trigger zone thus swallowing may bring on an attack

*Treatment* — The medical treatment of trigeminal neuralgia is usually without value Heat especially diathermy may produce considerable relief

The patient usually has to submit either to injection of the branches of the nerves or ganglion with absolute alcohol or to avulsion of the sensory root The injection with alcohol is also an important diagnostic procedure in distinguishing between trigeminal neuralgia and psychalgia The mortality following avulsion is less than 1 per cent and it results in few postoperative complications of which facial paralysis trophic disorders and deafness are the commonest Loss of sensation of course occurs in the distribution of the fifth nerve The operation is usually curative Recently Sjoqvist has advocated intramedullary tractotomy for relief of the intractable pain in the face

### Glossopharyngeal Neuralgia

The paroxysmal pain of this condition is similar to that seen in *tic douloureux* except for the distribution The pain radiates from the pharynx to the side of the neck and to the ear The pharynx and tonsil often act as a trigger zone and as a result swallowing frequently causes a paroxysm of pain Yawning may bring on a paroxysm The cause is unknown *The differential diagnosis* is to be made especially from trigeminal neuralgia Injection of the fifth nerve with alcohol will not produce a loss of pain if the condition is due to glossopharyngeal neuralgia Alcohol injection of the glossopharyngeal is hazardous because of the danger of injecting the vagus Avulsion of the root is curative and should be done intracranially The other types of neuralgia such as occipital brachial, intercostal and that of the lumbosacral regions usually have an organic basis behind them

### Coccygodynia

Neuralgia of the coccygeal nerves or coccygodynia in which the pain is referred *to the tip of the coccyx, which is tender,* is usually hysterical It comes on after trauma or childbirth and is aggravated by walking or sitting The proper treatment is psychotherapy Removal of the coccyx does not cure the condition unless it does so by its psychotherapeutic element

## LESIONS OF THE PERIPHERAL NERVES OF THE EXTREMITIES

### Ulnar Nerve

The ulnar nerve supplies the two inner heads of the flexor profundus digitorum the adductors of the thumb the inner head of the flexor brevis pollicis and the muscles of the hypothenar eminence the inner two lumbricales and all of the interossei The sensory part of the nerve supplies the palmar and dorsal surface of the little and the inner half of the ring finger and the inner side of the palm and back of the hand to a short distance above the wrist The nerve may be injured by direct trauma or by pressure such as for example pressure exerted on the deep *branch of the ulnar in* the palm or the pressure of leaning the elbows on a desk or chair The nerve may be *involved in a lesion of the brachial plexus* dislocation of a shoulder or elbow by pressure of splints fractures in or about the elbow, which later give rise to excessive callus formation The latter condition may cause an ulnar paralysis months or years after the primary injury Leprosy has a *special tendency* to involve the ulnar nerve If the injury is high flexion of the hand is weak and it is turned toward the radial side Extension of the distal phalanges and flexion of the proximal ones are impaired or lost so that claw hand (*main en griffe*) is formed due to unopposed action of the radial nerve Adduction of the fingers is impaired adduction of the thumb is *lost* Froment s sign is present This consists of a

flexion of the thumb when the patient tries to hold a piece of paper between his thumb and index finger, while an attempt is made to pull the paper away. The muscles supplied by the nerve waste. This is especially noticeable in the hypothenar eminence in the palm and the interosseous spaces which become hollowed out. Sensory loss corresponds to the anatomic distribution of the nerve and in mild cases is usually greater for touch than for any other form of sensation. Pain and paresthetic phenomena may be severe and vasomotor and trophic changes may cause distressing complications.

## SCALENUS COMPRESSION SYNDROME (SEE CHAPTER 24)

## THE MEDIAN NERVE

*The median nerve supplies the pronator* quadratus and the pronator radii teres the flexor carpi radialis the flexor sublimis the *two outer heads of the flexor profundus* digitorum the abductor and opponens of the thumb the flexor longus and part of the *flexor brevis pollicis and the two outer* lumbricales.

The sensory part of the nerve supplies the *outer part of the palm from the middle of* the ring finger to the thumb. On the dorsal aspect of the hand the nerve supplies the last *two phalanges of the index middle and* radial half of the ring fingers. The median is especially rich in trophic and vasomotor fibers. *The nerve may be affected anywhere* along its course for example by dislocation of the shoulder by bullet or stab wounds and it *may be involved as a part of a general* multiple neuritis. Depending on the level at which the nerve is involved the extent of the paralysis varies. Ordinarily implication of the nerve produces weakness of flexion at the wrist and flexion at the distal phalanges of the middle and index fingers especially the latter are greatly disturbed. The thumb is adducted and extended and the terminal phalanx of the thumb cannot be flexed. The thumb cannot be brought to touch the tips of the fingers. The thenar eminence and the pulps of the middle and index fingers and thumb become atrophic. Sensory loss is as a rule as great as the distribution of the nerve. Involvement of the median nerve usually produces a severe amount of burning pain which was designated by Mitchell as *causalgia*. It is a burning boring intractable pain which makes life unbearable. The nails in the distribution of the nerve become dry brittle and furrowed and the skin tense and glossy.

## MUSCULOSPIRAL NERVE (RADIAL NERVE)

This nerve supplies the triceps the anconeus, the brachioradialis, the extensors of the forearm and the long extensors of the *fingers and thumb*. The cutaneous distribution of the nerve varies. The posterior aspects of the hand not supplied by the median and *ulnar are innervated by the radial*. This is approximately the radial half of the dorsal aspect of the hand dorsal aspect of the *thumb of the index finger to the first* phalanx and the radial half of the middle finger to the first phalanx. The musculo*spiral nerve is frequently injured especially* by pressure in the axilla from a crutch during deep sleep especially a drunken one, *in which the weight of the head rests on the* humerus and presses against the nerve and by fracture of the humerus. It can also of *course be injured by bullet wounds or stab* wounds. The commonest cause is pressure on the nerve by drunken sleep the so-called Saturday night paralysis. Lead produces a double musculospiral paralysis *in which the supinator longus muscles are spared*. The paralysis which results from musculospiral palsy will depend upon the height of the injury to the nerve for example, if it is injured in the axilla there is paralysis in the entire distribution of the nerve including the triceps. The usual location of the involvement which is in the arm spares the triceps. There is paralysis of the extensors of the hand thumb and fingers the proximal phalanges of the latter being involved. The rest of the finger extension is done by the non paralyzed interosseous muscles. The forearm is pronated the wrist drops and the thumb is adducted flexed and opposed. The hand grip is weak if the patient attempts to grasp an object with the wrist dropped but if the hand is supinated

going remarks The presence of sensory findings will rule out organic affections of the ganglion and of the roots of the nerve The pain of *Sluder's neuralgia* is not limited to the fifth nerve and has a tendency to radiate to the shoulder, the importance and frequency of this has been greatly overestimated *In glossopharyngeal neuralgia* the pain radiates from the pharynx to the side of the neck and to the ear The tonsil may act as a trigger zone thus swallowing may bring on an attack

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hypertrophy may be seen. The wasted fibers are replaced by fibrous tissue and fat, producing myosclerosis. Pseudohypertrophy occurs in a form of the disease, especially implicating the deltoids and muscles of the calf. The muscles apparently enlarged have a hard inelastic feel. The age of onset is usually before ten years, but it may be delayed as late as twenty five years and cases have been reported even up to forty years of age. The amount of creatinine excreted daily is low. A diminished tolerance for creatine exists which bears some relation to the severity of the symptoms.

*Symptoms*.—The muscles involved are those of the trunk, the shoulder girdles, pelvic girdles, arms and thighs. The muscles below the elbows and below the knees may be affected early, but this is contrary to the rule and serves as one of the chief differential points between muscular dystrophy and the atrophies of the spinal origin. The face, while implicated in many cases, is not as a rule first involved. Due to involvement of the muscles of the hip and of the spine, the gait is of the so-called duck or waddling type and resembles, to a degree, that seen in double congenital dislocation of the hips. Weakness of the muscles of the spine causes distinct lordosis and great difficulty when the patient attempts to arise from a sitting position on the floor. The manner in which a patient with muscular dystrophy arises from the floor (he climbs up himself) is one of the most characteristic things in the disease, but may be seen in any patient who has weakness of the back and gluteal muscles from other causes. The involvement of the muscles of the shoulder girdles and the arms produces loose shoulders and winged scapulæ. As the muscles waste, their movements become weaker and gradually disappear. The same thing holds good for the deep reflexes. Sensation is normal and fibrillations are usually not seen. While the electrical reactions diminish and finally disappear, there are no reactions of degeneration. Some of the muscles may appear unusually large. This is due to replacement of the muscle with fat or connective tissue. In some cases actual hypertrophy of the muscle occurs. Such a muscle is harder than usual and yet may be weak to the point of paralysis. If the face is involved the so-called myopathic facies is seen. Wrinkles are absent, the folds are flattened out, tapir mouth ensues and the palpebral fissures are widened. All these symptoms are due to weakness in the distribution of the seventh nerves. The smile is a transverse one. The muscles are involved bilaterally and more or less symmetrically. The heart muscle has been involved in some cases. Contractures and ankylosis frequently occur, especially in patients who have very little attention paid to them in the line of physiotherapy. Some of the cases of dystrophy become freaks in the side shows of circuses. It is rare to have involvement of the tongue, ocular and jaw muscles.

The course of the disease is gradually progressive. Victims suffering from it are quite likely to be carried off by acute infections, but many live twenty to forty years after the onset. In some the disease progresses so very slowly that it appears to be arrested.

If it be borne in mind that the disease occurs early in life, chiefly in males, that the proximal segments of the limbs are affected, power, reflexes and electrical reactions gradually disappear, that there are no changes in sensation and that fibrillary tremors are unknown, there should be no difficulty in the diagnosis. Muscle biopsy is sometimes helpful.

There is no specific *treatment*. Massage and passive movements to the joints may prevent the occurrence of deformities. The use of glycine or glutamic acid has been disappointing as has been the results of vitamin E therapy.

## NEUROLOGY IN RELATION TO WAR

In addition to being subject to the same neurologic diseases as may afflict the civilian in peace time, the soldier in a global mechanized war is exposed to many hazardous conditions which tend to increase the incidence of neurologic disorders.

There are few if any neurologic diseases peculiar to war alone, but certain conditions occur much more frequently under war conditions than in civilian life and are worthy of brief mention.

the grasp will be good The sensory loss is not nearly so extensive as the distribution of the nerve, and, in many cases practically no sensory loss occurs

### Long Thoracic Nerve

This nerve supplies the serratus magnus It may be paralyzed from injury, carrying heavy weights on the shoulder and from inflammatory reactions The inferior angle of the scapula stands away from the chest and, on elevating the arm, the scapula becomes winged Weakness is encountered in raising the arm above the horizontal plane The lifting ability of the patient is diminished Pain is not usually present and the prognosis for recovery is fair

### Circumflex Nerve

This nerve supplies the deltoid and teres minor The sensory branch of the nerve supplies an oval space over the deltoid muscle If the nerve is completely involved the shoulder joint is relaxed the deltoid atrophic and the arm cannot be abducted Changes in electrical reactions occur Outward rotation of the arm is interfered with Pain is frequently severe and a loss of sensation occurs in the distribution of the nerve In arriving at a diagnosis, local conditions of the shoulder must be considered and ruled out

### External Popliteal

This is the external division of the sciatic and supplies the antero-external muscles of the leg the extensor longus digitorum the extensor proprius pollicis the tibialis anticus the peroneus brevis and the peroneus longus It innervates the skin on the dorsal surface of the first metatarsal and big toe, the antero-external surface of the leg and the dorsum of the foot including the dorsum of the great toe first second and third toes up to the second phalanges This nerve is frequently involved by direct injury especially as it winds around the head of the fibula, where it is susceptible to the pressure of a cast, to direct blows and to disease involving the upper part of the fibula It may be paralyzed as the result of occupation when the nerve is frequently squeezed, for example, in hardwood floor polishers and people who work in gardens and frequently bend the knees Crossing the legs for long periods especially in thin individuals also causes paralysis Lead involves the nerve bilaterally It is also occasionally injured in the pelvis during difficult labors Involvement of the nerve produces paralysis of the extensors of the foot and of the extensors of the proximal phalanges of the toes and impairment of eversion Foot drop, pes equinovarus and occasionally flat foot result Steppage gait on the affected side appears Contractures due to unopposed muscles may set in Pain, trophic and vasomotor changes are unusual and the cutaneous sensory loss is less than the supply of the nerve itself

*Treatment* —This will depend in a large measure upon the cause If there is evidence that the nerve has been directly injured by bullet wounds stab wounds or fracture or by pressure of the fragments of bone it should be investigated surgically as soon as possible although many patients with peripheral nerve injury complicated by complete paralysis of the nerve may make a total recovery without operation Some choose to wait six to twelve weeks before surgical interference If the nerve has been involved by pressure or infections or toxic cause surgical intervention is not indicated A splint or appliance should be made to support the muscles paralyzed Massage should be given daily or at least three times a week and faradism or galvanism applied to the affected nerve three times a week The outlook in pressure cases is usually good although the individual nerve may take from three to six months to recover Various orthopedic operations may produce more useful extremities if the nerve paralysis does not recover

## THE MYOPATHIES

### Progressive Muscular Dystrophy

This disease is strictly limited to the muscles The causes other than familial tendency to the disease are not known The nervous system, both central and peripheral is intact The muscle fibers show atrophy though occasionally a true

hypertrophy may be seen. The wasted fibers are replaced by fibrous tissue and fat, producing myosclerosis. Pseudohypertrophy occurs in a form of the disease, especially implicating the deltoids and muscles of the calf. The muscles apparently enlarged have a hard noneiastic feel. The age of onset is usually before ten years but it may be delayed as late as twenty five years, and cases have been reported even up to forty years of age. The amount of creatinine excreted daily is low, a diminished tolerance for creatine exists which bears some relation to the severity of the symptoms.

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Clinical and experimental data have shown that high explosive blasts may cause injury to the central nervous system without evidence of any external trauma. Lesions in the nervous system, particularly hemorrhages, were found at autopsy in soldiers dying after exposure to such blasts, while some men who recovered exhibited residual neurologic symptoms such as hemiplegia, paraplegia, pupillary and sphincter disturbances. In one group of 74 soldiers, 67 showed unmistakable signs of localized organic lesions of the central nervous system. Such signs often tended to be transient, having for the most part disappeared before a second examination a week later. Subdural hematoma and effusion have been reported as complications of high explosive blast injuries, on both land and in water. It is of interest that clinical neurologic abnormalities were not detected in approximately 80 per cent of the cases and the diagnosis depended mainly on psychiatric findings in the form of retardation in intellectual activity, and personality and mood disturbances. Some of the cases were erroneously diagnosed at first as war neurosis, traumatic neurosis or psychoneurosis. While we do not believe that all neuroses of war are due to structural disturbances of the nervous system, evidence such as the above suggests that many war neuro-psychiatric conditions blandly assumed to be due to anxiety, fright, "combat fatigue" and other emotional causes might likewise have a structural background if it were carefully sought after.

Another type of neurologic disturbance frequently encountered in war but rather rare in civilian life is the so-called reflex paralysis. In this condition rigidity and paralysis leading to immobilization of a limb and often accompanied by pronounced vasomotor disturbances occurred following an injury or wound in a remote part of the body. The cause of these reflex paralyses is still uncertain. Some consider them an hysterical manifestation, others as the result of immobilization or inactivity, while still others subscribe to the concept that disturbed sympathetic innervation is responsible.

### Causalgia

Causalgia, first described by Weir Mitchell in the Civil War, is likewise not infrequent following war injuries. In this condition following gunshot or other wounds involving certain peripheral nerves, especially the median and tibial, there occurs a characteristic paroxysmal type of pain in the injured member accompanied by severe trophic and vasomotor changes in the painful area. Jarring, air currents and emotional upsets may initiate the pain, while relief is afforded by placing the hand or foot in water. Some ascribe the condition to a disturbance of sympathetic regulating fibers, while Lewis suggests that the pain arises from irritation in the skin or peripheral nerve of nocifensor fibers which are a division of the posterior root system. Relief may be obtained in the early stages by local infiltration with procaine, paravertebral injections or sympathetic ganglionectomy. In the later stages these measures are of little avail and the pain persists even after rhizotomy and chordotomy.

### Phantom Limb

Following amputation of part of an extremity, especially an upper, the patient will frequently complain of discomfort, pain, itching and other disagreeable sensations in the part which has been lost. The symptoms are often extremely distressing; their cause is not absolutely determined, but it is likely that the brain misinterprets sensations arising from stimulation of the remaining stumps of the nerves as originating in the distal parts now lost. Treatment of this condition often is difficult. Occasionally resection of the nerve in the stump and sympathectomy will be helpful, but often more radical procedures such as excision of the parietal sensory cortex are necessary.

## REFERENCES


BAILEY PERCIVAL Intracranial Tumors 2nd ed Springfield Charles C Thomas 1948

BING R Textbook of Nervous Diseases St Louis C V Mosby Company 1939

GIBBS F A and GIBBS E L Atlas of Encephalography Cambridge Mass Lew A Cummings Company 1941

GIBBS F A GIBBS E L and LENNOX W G Electro-encephalographic Classification of Epileptic Patients and Subjects Arch Neurol and Psychiat 1943 *50* 111

MONRO D Thoracic and Lumbo-sacral Cord Injuries Jour Am Med Assn 1943 *122* 1055

MOORE M T Symptomatic Abdominal Epilepsy Am Jour Surg 72 883 1946

NIELSEN J M Agnosia Apraxia Aphasia 2nd ed New York Paul B Hoeber Inc 1946

ORNSTEEN A M Thrombosis of the Anterior Spinal Artery Am Jour Med Sci 1931, *181* 654

Poliomyelitis Papers and Discussions Presented at the First International Poliomyelitis Conference Philadelphia J B Lippincott Company 1949

POTTERFIELD T G and RUPP C Multiple Sclerosis A Clinical Review of 53 Autopsied Cases Diseases of the Nervous System 1948 *9* 355

WILSON G and RUPP C Present Trends in the Practice of Neurology J A M A 1947 *133* 509

WILSON G RUPP C and BARTLE H JR Ruptured Miliary Aneurysms Trans Am Neurol Assn 1941 *67* 40

WILSON G RUPP C and WILSON W W Dangers of Intrathecal Medication J A M A 1949 *140* 1076

WILSON S A K Neurology Baltimore Williams & Wilkins 1940

WOLFF H G Headache and Other Head Pain Oxford Univ Press 1948

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